Unmet Needs in Clinical Practice: A Proposal and Application of A Diagnostic and Severity Scale to Grade Cerebellar Mutism Syndrome

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Abstract

BACKGROUND: The post-operative Pediatric Cerebellar Mutism Syndrome (CMS) affects about one-third of children and adolescents following surgical removal of a posterior fossa tumor (PFT). According to the Posterior Fossa Society consensus working definition, CMS is characterized by delayed onset mutism/reduced speech and emotional lability after cerebellar or 4th ventricle tumor surgery in children, with additional common features that include hypotonia and oropharyngeal dysfunction/dysphagia. The main objective of this work was to propose a diagnostic scale to grade CMS duration and severity.

METHOD: Thirty consecutive subjects, aged 1-17 years (median 8 years, IQR 7) were evaluated with the proposed Post-Operative Pediatric CMS Survey after surgical resection of a PFT and, in cases of CMS, for the next 30 days after the onset (T_0) or until symptom remission. At day 30th (T_1), CMS was classified into mild, moderate, or severe according to the proposed Scale.

RESULTS: CMS occurred in 13 patients (43.3%, 95% C.I.: 25.5-62.6%), with mild severity in 4 cases (31%), moderate in 4 (31%), and severe in 5 (38%). At T_1 , longer symptom persistence was associated with greater severity ($p=0.01$). Greater severity at T_0 predicted greater severity at T_1 ($p=0.0001$). Children with a midline tumor location and those aged under 5 years at diagnosis were at higher risk of CMS ($p=0.025$ and $p=0.008$, respectively).

CONCLUSIONS: The proposed scale is a simple and applicable tool for estimating the severity of CMS at its onset, monitoring its course over time, and providing an early prognostic stratification to guide treatment decisions.

Declarations

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Key Points

1. Post-operative pediatric Cerebellar Mutism Syndrome (CMS) is a complex phenomenon with a wide spectrum of symptoms that may manifest in children undergoing the resection of a posterior fossa tumor (PFT) and that can result into long-term impairment and reduced quality of life
2. A diagnostic and severity scale to grade the duration and the severity of symptoms of the post-operative pediatric CMS, applicable in clinical practice and easy to be compiled by different health professionals, is here proposed
3. The association between the Total Severity Scale and Total Duration Scale scores, and that between the Total Severity Scale scores at T_0 and at T_1 could make it possible to estimate at the CMS onset the severity of its clinical course and provide an early prognostic stratification of patients to better guide decisions about rehabilitative treatment as well as to inform families regarding prognosis.

Importance Of The Study

The proposed scale for diagnosing and scoring of postoperative cerebellar mutism syndrome, designed for this study and based on the latest definition that emerged at the Consensus Meeting of the Posterior Fossa Society, has been shown to be an easy to use, applicable to clinical practice, and sensitive instrument to diagnose CMS in children, including those with a mild presentation. Formulating a scoring not only of the duration but also of the severity of cardinal symptoms allows a prognostic stratification to be made, which is critical for optimal planning of clinical and rehabilitative interventions. Thanks to the improvement in surgical techniques and co-adjuvant therapies available for the treatment of children with PFT, the survival-rate is increasing, and the standardization of diagnostic and prognostic criteria for CMS, as well as the development of a common clinical language between health professionals, can contribute to improve both clinical care and research activities.

Abbreviations

CMS Cerebellar Mutism Syndrome

PFT Posterior Fossa Tumor

PFS Posterior Fossa Society

Introduction

Post-operative pediatric Cerebellar Mutism Syndrome (CMS) is a complex phenomenon with a wide spectrum of symptoms that may manifest with different combinations and severity in children undergoing surgical resection of a posterior fossa tumor (PFT). These children may present with impairments in linguistic, cognitive, motor, and affective/behavioral functioning. The core symptom of the syndrome is mutism, defined as a severely reduced speech production, limited to single words or short sentences elicited only after vigorous stimulation¹. On average, mutism occurs within two days post-operatively, but may not present for up to 7 days². Although mutism is always transient and recovers spontaneously, long-term dysarthria or other higher language impairments often persist³. Another remarkable feature of this condition is emotional lability, which is characterized by exaggerated changes in mood or affect with a rapid fluctuation of emotional expression^{4,5}. The overall estimated incidence of the syndrome in children with PFT is between 11% and 30%, depending on the different presentations of tumor types⁶. Several risk factors have been associated with CMS, with different levels of evidence. Medulloblastoma tumor type, tumor location in the cerebellar midline, tumor location in the fourth ventricle, and brainstem involvement are well-established risks factors⁷. There are unconfirmed reports of other possibly significant risk factors, including younger age, left-handedness⁸, pre-operative language impairment^{9,10} and a lower socioeconomic background¹¹. Other factors such as sex, pre-operative hydrocephalus and extent of the resection do not seem to contribute to the risk of CMS¹². For several years, confusion has encompassed the description of post-operative cerebellar mutism and its associated clinical features, as shown by the heterogeneous terminology often used to describe the syndrome⁶. Moreover, no international guideline to date defines the diagnosis, prevention, treatment, or follow-up of this disabling condition¹³. For these reasons, in 2014 the Posterior Fossa Society (PFS) was funded to systematically gather and exchange information on the syndrome. The PFS is an international and multiprofessional group of expert neurosurgeons, neurologists, child neuropsychiatrists, neuroradiologists, neuropsychologists, speech therapists and neuroscientists with a particular interest in post-operative CMS. In 2015 the PFS initiated an international consensus process, motivated by the purpose of improving quality of life of pediatric brain tumors patients. This consensus process aimed to create a new formal and shared definition of the condition, define standardized methods for the diagnosis and follow-up, and monitor acute and late sequelae.

In the consensus paper, the PFS proposed a new working definition of the post-operative pediatric CMS, defined as characterized by delayed onset mutism/reduced speech and emotional lability after cerebellar or 4th ventricle tumor surgery in children, with additional common features that include hypotonia and oropharyngeal dysfunction/dysphagia. It has been highlighted that the CMS may frequently be accompanied by the cerebellar motor syndrome, the cerebellar cognitive affective syndrome, and brain

stem dysfunction including long tract signs and cranial neuropathies¹³. In this paper, the PFS pointed out the need for developing a new CMS scoring scale for the diagnosis of the syndrome, to measure not only the duration of post-operative symptoms, as in the CMS survey by Robertson et al. (2006), but also their severity, which is correlated with the long-term impairment of these children¹⁴. This tool may be useful to identify CMS-positive patients that should receive a full multiprofessional assessment for the purpose of rehabilitation. During the third Consensus Meeting of the PFS, held in Reykjavik in 2018, the need of a new evaluation scale of CMS was reiterated¹⁵, possibly designed to be:

- administrable as soon as possible after surgery, in order to catch the real delay in the onset of symptoms;
- formulated in a simple and easy to complete way, considering the critical issues of the post-operative phase;
- administrable by a variety of different health professionals (e.g., medical doctor, nurse, speech therapist).

The importance of recording latency of onset, duration, and symptom severity (not assessed in the scale by Robertson et al.) was emphasized as a means of making a prognostic stratification and guiding treatment.

The aim of this work was to propose a diagnostic and severity scale that grades the duration and severity of the symptoms of the post-operative pediatric CMS, and is easily implementable in clinical practice. According to the key points suggested during the third Consensus Meeting of the PFS, the scale was designed to be easily administered by different health professionals, such as neuropsychologists, medical doctors and nurses. A secondary aim was to estimate the incidence rate of CMS, applying broader diagnostic criteria. Another purpose of this study was to obtain a better definition of the individual characteristics of patients with post-operative CMS in our sample, for future prognostic categorization and stratification to inform clinical-rehabilitative therapeutic plans.

Materials And Methods

Study design

This was a single-centre prospective cohort study of clinical data obtained from children who underwent surgery for a PFT between 2017 and 2021. The study was carried out in accordance with the ethical principles enshrined in the Helsinki Declaration and was approved by the institution's research ethics committee. A written informed consent to study participation by parents or legal guardians was collected.

Participants

Patients aged 1-17 years, admitted at the Pediatric Neurosurgery Unit of the Children's Hospital "Regina Margherita" of Turin between September 2017 and March 2021, with a diagnosis of posterior fossa tumor, made with preoperative conventional MRI, who underwent a neurosurgical intervention by removal (total, partial or biopsy), were included. Patients with known pre-morbid neuropsychiatric diagnoses or severe complications in the post-operative period were excluded. Additionally, the surgical reports were reviewed to determine the extent of resection.

According to the standard protocol of the hospital, each patient received a comprehensive neurosurgical and neurological examination at the admission and brain MRI scans during the pre-operative period. The neurosurgical removal operation was assisted by the intraoperative neurophysiological monitoring for all patients. In the post-operative period, each child received neurosurgical, neurological, and oncological examinations and MRI scans. In addition, the participants underwent a clinical evaluation by completing the "Post-operative pediatric CMS survey" immediately after surgery, and for the next 30 days or until symptoms remission. Symptom scoring was done after the observation of the patient by the clinician or, if not possible, the staff (nurses, physiotherapists) were asked to report symptoms and parents were asked to describe symptoms.

Patients' demographics as well as their neurological and language development history were collected. Pre-resection neurological functioning and speech were clinically assessed, pre-resection MRI data (tumor localization, invasion or compression of the brainstem and the presence of hydrocephalus), post-resection clinical information (latency, severity, and duration of the CMS symptoms), post-resection MRI data (extent of resection), and post-resection histology information (classified according to the 2016 WHO System) were collected. The extent of tumor resection was based primarily on the postoperative MRI report and/or images, supplemented with the surgeon's estimate as detailed in the operative report. Extent of tumor resection was classified as follows: "Total": the MRI and surgeon indicated complete resection; "Subtotal": > 90% of the tumor removed; "Partial": < 90% of the tumor removed; "Biopsy": no significant change in the size of tumor postoperatively. Patient's characteristics of the sample are summarized in Tables 1 and 2.

The CMS Survey and Scale

The diagnostic and scoring scale for post-operative CMS was designed after a thorough review of existing literature on the subject. The survey assesses the presence and the time of onset of the syndrome, as well as the duration and the severity of the four symptoms, considering the latest definition of CMS, formulated at the Consensus Meeting of the PFS. Mutism and emotional lability (cardinal symptoms of the syndrome), hypotonia and dysphagia (additional symptoms) have been included in the survey. Mutism was considered as the only necessary and sufficient symptom for CMS diagnosis. Not only the absence but also a quantitative and qualitative change from pre-surgical speech production was classified as mutism symptoms¹³. As suggested during the Consensus Meeting of 2018, the scoring system had been reviewed with all the staff, to make it sure it was simple, clear, feasible by different

professional figures and not only by the specialist medical doctor. The post-operative pediatric CMS survey was administered immediately after surgery and, if CMS occurred, for the next 30 days or until the remission of symptoms (Online Resource 1). For each of the four symptoms of the CMS Survey (Mutism, Emotional Lability, Hypotonia and Dysphagia) a final score was assigned to duration and severity. The severity final score corresponded to the highest score achieved in the first 30 days. A scoring system was proposed for assessing CMS duration and CMS symptom intensity, both contributing to an overall CMS severity score (Fig. 1).

Data analysis

Descriptive analyses were applied to the data: categorical variables were expressed in absolute and percentage values, and continuous variable as medians and interquartile ranges (IQR). Based on the literature data ^{16,17}, age was dichotomized into two classes (class 1: less than/equal to 5 years; class 2: over 5 years). The variable “tumor type”, composed by seven classes corresponding to the histological typing of the tumor, was dichotomized for analytical purposes into “medulloblastoma/other aetiology”. Similarly, the variable “tumor localization”, composed by five classes, was dichotomized into “involvement/non-involvement of the structures of the midline (cerebellar worm, IV ventricle)”. Stratified data analyses were performed for cerebellar mutism syndrome. The Fisher’s Exact Test or the Fisher-Freeman-Halton Test, when appropriate, was used to measure association between categorical variables. Mann-Whitney U test was used for the association analysis of the continuous variable “age at diagnosis”. Statistical significance was set at $\alpha \leq 0.05$ (two tailed). Statistical processing was performed using IBM SPSS Statistic software, version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Sample demographics, clinical characteristics

Thirty-one children were enrolled in this study between September 2017 and March 2021. All patients underwent surgical resection of a posterior fossa tumor. One patient was excluded because of severe complications in the post-operative period. Therefore, the sample consisted of 30 patients (19 males and 11 females), with a median age of 8 years (IQR 7) at T₀. Twelve patients (40%) were aged under 5 years at the time of enrollment. Assessment of pre-operative speech behavior showed deficits in 7 patients (23%). The most common tumor types were pilocytic astrocytoma (50%), medulloblastoma (20%), diffuse astrocytoma (10%), and ependymoma (10%). The tumor was located at the midline in 15 cases (50%), with brainstem invasion in 8 children (27%) and a compression of it in 12 cases (40%). At the time of the PFT diagnosis, 25 patients (83%) had hydrocephalus (Table 2).

CMS Subgroup

CMS was diagnosed in 13 (43.3%, C.I. 95%: 25.5-62.6%) out of the 30 assessed (7 males and 6 females), with a median age of 4 years (IQR 6) at the onset of the symptoms (T_0). Nine patients (69%) were under 5 years of age at diagnosis. Assessment of speech behavior showed deficits in 3 (23%) patients. The CMS occurred in 3 out of 6 children with a diagnosis of medulloblastoma, 3 out of 3 with an ependymoma, 6 out of 15 with a pilocytic astrocytoma and 1 out of 3 with diffuse astrocytoma. The tumor was located at the midline in 10 patients (77%). In 3 children who developed CMS, tumor invaded the brainstem (23%), and in 5 compressed it (38%). Eleven children who developed CMS (85%) had a preoperative hydrocephalus. Additionally, operative reports were reviewed to determine the extent of resection: of the 13 children diagnosed with CMS, 9 (69%) had a complete resection and 4 had residual tumor documented by postoperative MRI.

Comparison between patients with CMS and without CMS

Association analyses showed a significant difference in age at diagnosis, with a higher occurrence of CMS in younger patients (median 4 years of age, IQR 6) compared to the older ones (median 9 years, IQR 6) ($p = 0.004$, Mann-Whitney test, Figure 2). Based on data in the literature¹⁶, this difference was further investigated by making a dichotomization of the variable "age at diagnosis" into two classes (less than or equal to 5 years vs. over 5 years). Results showed a significantly higher frequency of CMS in the younger age class ($p=0.008$, Fisher's exact test).

A higher frequency of CMS was found also in the subgroup of patients with a midline location of the tumor compared to other locations ($p=0.025$, Fisher's Exact test). No statistically significant correlation was found with the other investigated variables (Table 1).

Post-Operative Pediatric CMS Scale

The spectrum of CMS symptoms in the study children varied from transient mutism without neurobehavioral symptoms to mutism with severe behavioural symptoms of longer duration. Mutism emerged immediately after surgery in 2 (15%) patients, after 1-2 days in 8 patients (62%) and after 2-4 days in 3 (23%) patients. The duration of the mutism varied from 5 days to 5 months. In 11 patients (85%), characteristic behavioural CMS symptoms were associated with the severe reduction in spontaneous speech. Emotional lability lasted more than four weeks in one patient, while in the others it resolved within a month. Hypotonia was the most frequent and severe symptom, with a longer remission time compared to the others (more than a month). Dysphagia resolved within the first 25 days in 5 patients, although in 4 patients it lasted more than a month, with a gradual decrease in severity score.

After 30 days from the surgical resection (T_1) the overall scales were scored. According to the CMS scoring system proposed, the intensity of the syndrome was judged to be mild in 4 (31%) patients with CMS, moderate in 4 (31%), and severe in 5 (38%). Detailed results are shown in Table 3.

The scores of symptoms in the "duration" and "severity" scales were rather homogeneous for each patient (the same or only 1-point discordant). When discordant, the duration score was higher than the

severity score. A significant number of patients still had deficits after one month: 69.2% (9/13) had severe hypotonia, 23.1% (3/13) had severe mutism, 30.8% (4/13) had dysphagia, of moderate severity in 2 cases and severe in the other 2, and 15.4% (2/13) had emotional lability, of mild severity in one case and severe in the other.

Association analyses were performed to evaluate the possible clinical application of a symptoms severity scale, administered daily since the first day after surgery, to estimating syndrome duration. It emerged that higher scores on the "Total Severity Scale" corresponded to higher scores on the "Total Duration Scale" in a significant way ($p = 0.012$, Fisher-Freeman-Halton test). After a further dichotomization of severity and duration into two classes (i.e., class one: patients with mild or moderate scores (1 or 2) and class two: patients with severe scores (3)), it was found that class two-patients obtained higher scores on the "Total Duration Scale" compared to class one-patients ($p=0.005$, Fisher's Exact test, Figure 3). Furthermore, it emerged a significant association between the "Total Severity Scale" scores at T_0 and at T_1 , with higher severity scores at T_0 corresponding to higher severity scores at T_1 ($p=0.0001$ Fisher-Freeman-Halton test).

Discussion

The main goal of this work was to propose a diagnostic and scoring survey that could be used to identify and grade CMS. Following the recommendation to ensure feasibility emerged at the Consensus Meeting of the PFS in 2018, the proposed scoring scale is brief and easily administrable.

The advantage of this survey is that it could represent a standardized method for the diagnosis of CMS based on a shared definition, including mutism, emotional lability, hypotonia and dysphagia. Formulating a scoring not only of the duration but also of the severity of these cardinal symptoms makes the scale very sensitive, allowing the diagnosis of even mild CMS presentations. The periodical compilation of the survey, starting from the immediate post-operative, allows a prognostic stratification of patients, fundamental for the consequent planning of clinical-rehabilitative therapeutic interventions.

The sample analysis showed that the scores of the "Total Severity Scale" and the "Total Duration Scale" are associated, with higher severity corresponding longer duration. Even more interesting is the result that higher scores of Total Severity determined at T_0 are associated with higher scores of Total Severity Scale determined at T_1 . If these analyses are confirmed by future studies with a larger sample size, having a tool to estimate the severity of CMS from presentation would allow an early prognostic stratification of patients to be made for better guiding clinical decisions about rehabilitative treatment as well as informing families about prognosis in a more detailed way. In particular, the early identification not only of patients with severe CMS but also of patients with mild or moderate CMS, would allow the initiation of an early intensive rehabilitation treatment to improve the overall prognosis¹⁵.

We encountered greater difficulties with hypotonia, for which there is no standardized rating scale. Using a severity subdivision (e.g., mild / moderate / severe) would have made the score extremely subjective

and difficult to compare between different observers. Therefore, we decided to grade it by defining the extent of the hypotonia ("ipsilateral" / "affects the four limbs" / "affects the four limbs and the trunk"), but this aspect could be improved.

Although we succeeded in administering the scale to our sample of children with PFT during the post-operative period, and the scale seemed feasible to be used in routine clinical practice, we have to underline that frequently a multiprofessional discussion was needed to define the severity of symptoms, especially for hypotonia and dysphagia.

A secondary aim of the work was to define the individual characteristics of patients suffering from post-operative CMS for a prognostic categorization and stratification. There was no sex influence in CMS development in our series. Pre-operative speech disorders were similarly represented among those with or without CMS. In line with the risk factors already reported in the literature, patients who developed CMS were numerically more likely to have a medulloblastoma, infiltration or compression of the brainstem, total tumor resection, or pre-operative hydrocephalus. However, these differences were not statistically significant, presumably due to the small sample of enlisted patients. The only features for which a statically significant correlation was found were tumor location and age at diagnosis. These observations are congruent with the current literature.

Another secondary aim was to investigate the diagnostic implications of the broader criteria for CMS that were suggested by the consensus meeting of the PFS¹⁵. Based on our sample, the estimated incidence was larger than most previously reported rates (43.3 %, C.I. 95%: 25.5-62.6% in our sample vs. 11-30% in the literature)⁶. This difference could be due to the application of the scale in the immediate post-operative, not only evaluating duration of symptoms in patients with total absence of language but also considering milder symptoms (i.e., qualitative and quantitative reduction of speech) as sufficient for diagnosis¹³. This might have led to a greater diagnostic sensitivity. As proof of this, the prevalence of CMS classified as "severe" in our sample was 16.7%, whereas the prevalence of CMS with moderate or severe symptoms was 30%, which is consistent with the data reported in the literature. It is therefore possible that the prospective compilation of the diagnostic and scoring scale from the immediate post-operative involves greater diagnostic sensitivity, also including those patients with short-lived and mild intensity symptomatology, which may not be detected when the diagnostic interview is compiled retrospectively. As already reported, latency before onset of symptoms could be affected by sedation and mechanical ventilation after surgery, so that symptoms were noted only after the sedation was stopped and the tracheal tube removed.

Finally, because of the limited sample size and single site design, and the non-standardized scaling of the severity of the symptoms of CMS, this study should be considered as a preliminary qualitative investigation aimed at exploring the utility and feasibility of the instrument. Indeed, future studies will be needed to quantitatively explore the sensitivity of this battery in detecting cerebellar symptoms typical of CMS and to validate the tool in a larger multicentre cohort of patients with posterior fossa tumours.

Conclusions

The scale of diagnosis and scoring of postoperative cerebellar mutism syndrome, designed for this study and based on the latest definition that emerged at the Consensus Meeting of the Posterior Fossa Society in 2015, has been shown to be simple and applicable in clinical practice. The compilation of the data collection survey, carried out periodically starting from the immediate post-operative, makes the scale very sensitive, allowing the diagnosis of even mild CMS presentations. Formulating a scoring not only of the duration but also of the severity of cardinal symptoms can provide clinician and researchers with a useful tool for prognostic stratification, which is critically important for optimal planning of the clinical-rehabilitative therapeutic activities. Thanks to the improvement of surgical techniques and co-adjuvant therapies available to treat children suffering from posterior cranial fossa tumor, their survival-rate is increasing, thus making it essential to think about targeted rehabilitation plans. The standardization of the diagnostic and prognostic criteria of CMS, and the development of a common clinical language between clinical centers and health professionals can benefit both the clinical care of these patients and future research activities.

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Tables

Due to technical limitations, Tables are only available as a download in the Supplemental Files section.

Figures

TIME OF pCMS ONSET:

- 1 = immediately after surgery;
 2 = 1-2 days after surgery;
 3 = 2-4 days after surgery;
 4 = ≥ 4 days after surgery.

CARDINAL pCMS SYMPTOMS:**A) MUTISM**

DURATION: ____	SEVERITY: ____ *
1 = <1 week 2 = 1-4 weeks 3 = ≥ 4 weeks	1 = Short sentences 2 = Single words 3 = Total absence of verbal production *For children <3 years consider quantitative reduction of the pre-operative acquired language milestone or regression to a prior language milestone

B) EMOTIONAL LABILITY

DURATION: ____	SEVERITY: ____
1 = <1 week 2 = 1-4 weeks 3 = ≥ 4 weeks	1 = Emotionality congruous / low threshold, containable states of agitation 2 = Emotional sometimes congruous and sometimes incongruous / Low-threshold, poorly contained agitation states 3 = Incongruous emotionality / Incongruous states of agitation

C) HYPOTONIA

DURATION: ____	SEVERITY: ____
1 = <1 week 2 = 1-4 weeks 3 = ≥ 4 weeks	1 = Ipsilateral 2 = Affects the four limbs 3 = Affects the four limbs and the axis

D) OROPHARYNGEAL DYSPHAGIA

DURATION: ____	SEVERITY: ____
1 = <1 week 2 = 1-4 weeks 3 = ≥ 4 weeks	1 = Liquid dysphagia 2 = Dysphagia for chewing foods 3 = Complete dysphagia

Cerebellar Mutism Syndrome (1 = yes; 2 = no; 9 = uncertain): ____

SCORING:

TOTAL DURATION SCALE: ____	TOTAL SEVERITY SCALE: ____	OVERALL SEVERITY SCALE: ____
3= Severe (at least two symptoms of duration 3) 2 = Moderate (at least two symptoms of duration 2 or a symptom of duration 3 and at least one of duration 2) 1 = Mild (all other combinations)	3= Severe (at least two symptoms of severity 3) 2 = Moderate (at least two symptoms of severity 2 or a symptom of severity 3 and at least one of duration 2) 1 = Mild (all other combinations)	3= Severe if both scales ("duration scale" and "severity scale") are severe 2 = Moderate if both scales are moderate or if one is severe and one is moderate; 1 = Mild (all other combinations)

Figure 1

Pediatric Post-Operative CEREBELLAR MUTISM SYNDROME (pCMS) Scale

Figure 2

Side-by-Side (Comparative) Box-Plot of age at tumour diagnosis by pCMS. In the sample, patients without pCMS (“No” CMS group) were older at time of tumour diagnosis compared with patients who developed pCMS (“Yes” CMS group). The median age at tumour diagnosis for the “Yes” pCMS group was 4 years-old (IQR 2-6, min 1-max 10), compared to 9 years-old (IQR 8-13, min 3-max 17) for “No” pCMS group.

Figure 3

Duration and Severity Scatter-plot. “Total Severity Scale” and “Total Duration Scale” scores were each categorized into two severity classes: class one patients with moderate and mild scores (1/2), class two patients with severe scores. In the sample, higher scores on the “Total Severity Scale” corresponded to higher scores on the “Total Duration Scale”.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [OnlineResource1.pdf](#)
- [ricci.Tables.pdf](#)