Does the mesodermal derangement in Chiari Type I malformation extend to the cervical spine? Evidence from an analytical morphometric study on cervical paraspinal muscles

Sumit Thakar, MCh, Avinash Kurudi Siddappa, MS, MCh, Saritha Aryan, MS, MCh, Dilip Mohan, MS, MCh, Narayanam Anantha Sai Kiran, MCh, and Alangar S. Hegde, MCh, PhD

Department of Neurological Sciences, Sri Sathya Sai Institute of Higher Medical Sciences, Bangalore, India

OBJECTIVE The mesodermal derangement in Chiari Type I malformation (CMI) has been postulated to encompass the cervical spine. The objectives of this study were to assess the cross-sectional areas (CSAs) of cervical paraspinal muscles (PSMs) in patients with CMI without syringomyelia, compare them with those in non-CMI subjects, and evaluate their correlations with various factors.

METHODS In this retrospective study, the CSAs of cervical PSMs in 25 patients were calculated on T2-weighted axial MR images and computed as ratios with respect to the corresponding vertebral body areas. These values and the cervical taper ratios were then compared with those of age- and sex-matched non-CMI subjects and analyzed with respect to demographic data and clinicoradiological factors.

RESULTS Compared with the non-CMI group, the mean CSA values for the rectus capitis minor and all of the subaxial PSMs were lower in the study group, and those of the deep extensors were significantly lower ($p = 0.004$). The cervical taper ratio was found to be significantly higher in the study cohort ($p = 0.0003$). A longer duration of symptoms and a steeper cervical taper ratio were independently associated with lower CSA values for the deep extensors ($p = 0.04$ and $p = 0.03$, respectively). The presence of neck pain was associated with a lower CSA value for the deep flexors ($p = 0.03$).

CONCLUSIONS Patients with CMI demonstrate alterations in their cervical paraspinal musculature even in the absence of coexistent syringomyelia. Their deep extensor muscles undergo significant atrophic changes that worsen with the duration of their symptoms. This could be related to a significantly steeper cervical taper ratio that their cervical cords are exposed to. Neck pain in these patients is related to atrophy of their deep flexor muscles. A steeper cervical taper ratio and alterations in the PSMs could be additional indicators for surgery in patients with CMI without syringomyelia.

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KEY WORDS cervical paraspinal muscles; morphometry; Chiari Type I malformation

CHIARI Type I malformation (CMI) is a mesodermal disorder characterized by an abnormal caudal descent of the cerebellar tonsils through the foramen magnum. The pathophysiological spectrum of the disorder is attributed to altered CSF pressure dynamics in the spinal subarachnoid space and the spinal cord. The ensuing changes in the anterior and/or posterior horn cells have been demonstrated by the occurrence of denervation in the cervical paraspinal muscles (PSMs) in patients with CMI and syringomyelia.²³ However, changes in the cer-

vical PSMs have not been assessed in patients with CMI in the absence of coexistent syringomyelia. The evaluation of cervical PSMs in CMI gains significance, given that neck pain is a common symptom in this disorder and that alterations in cervical PSM morphology have been reported to be significantly correlated with this symptom.^{9,14} Furthermore, it has also been postulated that the mesodermal derangement in CMI extends to the subaxial cervical spine,^{7,8,24} and it is not known whether these changes involve the cervical PSMs as well.

ABBREVIATIONS CMI = Chiari Type I malformation; CSA = cross-sectional area; CVJ = craniovertebral junction; DE = deep extensor; DF = deep flexor; ICV = intracranial volume; OCA = occipital condyle area; PFV = posterior fossa volume; PSM = paraspinal muscle; RCma = rectus capitis major; RCmi = rectus capitis minor; SE = superficial extensor; SF = superficial flexor; VBA = vertebral body area; WAD = whiplash-associated disorder.

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FIG. 1. T2-weighted axial MRI section demonstrating the regions of interest used in measurement of the CSA of the subaxial PSMs. VB = vertebral body.

Methods

Patient Population

Records from a total of 40 symptomatic patients with primary CMI (demonstrating a tonsillar herniation ≥ 5 mm below the foramen magnum without any predisposing cause for the same) without syringomyelia, who underwent foramen magnum decompression and duraplasty between 2008 and 2012, were screened. The study cohort was a homogeneous group of 25 patients whose preoperative MR images were stored in the hospital imaging system and who did not have scoliosis, any coexisting bony craniovertebral junction (CVJ) anomaly, any cervical pathology, or any history of surgery in the CVJ or cervical regions. Patients with features of a “presyrinx” condition were excluded from the study.

Comparison Group

Twenty-five age- and sex-matched non-CMI subjects were selected from the neurosciences outpatient department for comparison of their cervical PSM morphometry and cervical taper ratio with that of the study group. These subjects did not report neck or radicular pain nor previous neck trauma or surgery, and had undergone cervical spine MRI as part of a screening protocol during their neurological evaluation.

Radiographic Evaluation

The same imaging protocols were used for measurements in both the comparison and study groups. The cross-sectional area (CSA) measurement method was based on the technique standardized in previous studies.^{1,21} Digital images of the preoperative cervical spine MRI were retrieved from the hospital radiographic system (Synapse, Fujifilm Health Systems). MR images were acquired on an HDi 1.5-T magnet (GE Signa) using a standard neurovascular coil. Measurement parameters were as follows: slice

FIG. 2. T2-weighted axial MRI scans demonstrating measurement of the CSA of the RCmi (left) and RCma (right). OC = occipital condyle.

es 26; slice thickness and space 3.7 mm; FOV 180 × 188 mm; TR 4360 msec; TE 98.2 msec; matrix size 1.60/256, number of excitations 1.5; and flip angle 90°.

Measurements for the suboccipital muscles (rectus capitis posterior minor [RCmi] and rectus capitis posterior major [RCma]) were taken at occiput–C1 for the RCmi muscle after identifying the dens and occipital condyles and at the most cephalad portion of the C-2 vertebral level for the RCma muscle on axial sections of conventional T2-weighted spin-echo images. For the measurement of the subaxial PSM areas, axial sections at the upper vertebral endplates from C-3 to C-7 taken parallel to the disc spaces were used. The measured flexors included the sternocleidomastoid (superficial flexor [SF]), and the longus colli and longus capitis (deep flexors [DFs]). The extensors included the multifidus and semispinalis cervicis (deep extensors [DEs]); and the semispinalis capitis, splenius capitis, and upper trapezius (superficial extensors [SEs]) (Fig. 1). The CSA measurement was performed by creating a region of interest for each muscle bilaterally. Perpendicular lines from the lateral border of the facets were used as lateral limits for the region of interest for the SEs.

Muscle CSA/bony CSA ratios rather than absolute muscle CSA values were used to eliminate biases arising from variations in the build of the patient. This was based on a previously used assumption that the muscle areas biomechanically correspond to the morphometry of the bone at any given level.²¹ The occipital condyle areas (OCAs) were used for the calculation of this ratio for the RCmi area values (Fig. 2 left), whereas the vertebral body areas (VBAs) at the cuts taken for measurement of the muscle areas were used for the RCma (Fig. 2 right) and subaxial muscle area values (Fig. 1).

Two consultant neurosurgeons (S.T. and A.K.S.) functioned as independent observers for all measurements. They were blinded to the clinical history, the radiologist's report at the time of imaging, and the group allocation into cases and control subjects. The parasagittal MRI sequences demonstrating the tonsillar position were not provided to them during the CSA measurements. The mean of the sum of the muscle CSAs on either side at all levels, and the means of the PSM CSA/bony CSA ratios were then calculated as follows: RCmi CSA/OCA, RCma CSA/VBA, SF CSA/VBA, DF CSA/VBA, SE CSA/VBA, DE CSA/VBA, DF CSA/DE CSA, and SF CSA/SE CSA. The mean values of the PSM CSA/bony CSA ratios recorded by the 2 observers were used for analysis.

The measurement of the cervical taper ratio (tapering of the anteroposterior spinal canal dimension from C-1 to

TABLE 1. Radiological characteristics of the study cohort

Variable	Mean $\pm$ SD	Min	Max
PFV/ICV ratio	0.15 $\pm$ 0.02	0.11	0.18
Tonsillar herniation (mm)	13.26 $\pm$ 7.35	5.70	29.89
Taper ratio	0.84 $\pm$ 0.51	0.13	2.10

C-7) was done by a previously described technique.⁸ Lines placed perpendicular to the spinal canal at the midpoint between the top and bottom of each vertebra on the T2-weighted sagittal MRI sequences were measured as the anteroposterior diameter of the spinal canal and plotted against the spine levels. A trend line was fitted by linear regression to the diameters between C-1 and C-7, and the slope of this line was recorded as the cervical taper ratio (mm/level). The posterior fossa volume (PFV) and intracranial volume (ICV) were measured as described previously.⁶

Statistical Analysis

Using the formula for sample size calculation for paired means and incorporating the clinically meaningful difference in CSA values from a previous study on cervical PSMs,²¹ a sample size of 25 was determined to be adequate to obtain a power of 0.9 for the study. Data were entered in an Excel spreadsheet (Microsoft, Inc.) and analyzed using SPSS version 20. Means and standard deviations were computed for continuous variables. The Student t-test was used to compare differences between the area ratios in the comparison and study groups, and for the subgroup analysis based on the absence or presence of neck pain.

Correlation of various continuous variables (age, duration of symptoms, PFV/ICV, tonsillar herniation, and taper ratio) with the muscle area ratios was analyzed using

the Pearson's correlation test. An ANOVA was used to analyze the effect of categorical variables (sex, presence or absence of neck pain, and CSF flow on cine MRI) on the muscle area values. A linear regression analysis was performed to predict the muscle area ratios from various clinical and radiological factors. Interobserver variability was measured using the intraclass correlation coefficient and standardized ratings of agreement.¹¹

Results

Demographic Data and Radiological Characteristics

There were 14 males and 11 females in the study group; their mean age was 30.90 $\pm$ 13.52 years (range 9–56 years). The comparison group had identical sex and age characteristics. The mean duration of symptoms was 34.08 $\pm$ 42.40 months (range 3–180 months). Twelve (48%) patients complained of neck pain at presentation. None of the patients had scoliosis. The radiological findings of the cohort are listed in Table 1.

Muscle Areas in Control Versus Study Groups

Compared with the non-CMI comparison group, the mean PSM/bony area ratio for RCmi and all of the subaxial muscles was lower in the study group, whereas the RCma CSA/VBA ratio was higher (Fig. 3). Of these values, the mean DE CSA/VBA ratio was significantly lower in the study group ($p = 0.04$). Figure 4 compares the muscle areas in a 35-year-old male patient with those of an age- and sex-matched control subject.

Cervical Taper Ratios

The cervical taper ratio (C1–7) was -0.39 ± 0.24 mm/level for the comparison group (Fig. 5 right) and -0.84 ± 0.52 mm/level for the study group (Fig. 5 left). The difference between these values was significant ($p = 0.0003$).

FIG. 3. Bar graph comparing the mean PSM area/bony area ratios in the control subjects and patients.

FIG. 4. Illustrative example comparing PSM areas in a 35-year-old man with those in an age- and sex-matched control. T2-weighted axial MRI sections demonstrate a larger RCmi area in the control subject (A) than in the patient (B), a smaller RCma area in the control subject (C) than in the patient (D), and larger areas of the subaxial muscles in the control subject (E) than in the patient (F).

Muscle Areas in Relation to Neck Pain Status

The mean muscle areas of CMI subgroups with and without neck pain were compared with those of the non-CMI comparison group (Table 2). The subgroup of patients with CMI with neck pain demonstrated a smaller mean DF CSA/VBA ratio compared with that of the non-CMI group ($p = 0.05$). Compared with the non-CMI group, the

DE CSA/VBA ratio was significantly smaller in both of the CMI subgroups ($p < 0.05$).

Bivariate Analysis

Pearson's correlation analysis (Table 3) demonstrated a strongly negative correlation of duration of symptoms with the DE CSA/VBA ratio ($r = -0.54$). The cervical taper ratio demonstrated a strongly positive correlation with the SE CSA/VBA ratio ($r = 0.65$), a moderately positive correlation with the DF CSA/DE CSA ratio ($r = 0.45$), and a strongly negative correlation with the SF CSA/SE CSA ratio ($r = -0.53$). There was no significant correlation of sex, presence or absence of neck pain, and CSF flow on cine MRI with any of the muscle ratios ($p > 0.05$).

Multiple Regression Analysis

A linear regression analysis was performed to evaluate the influence of age, sex, duration of symptoms, PFV/ICV, CSF flow on cine MRI, tonsillar herniation, taper ratio, and presence of neck pain on the PSM CSA/VBA ratios (Table 4). Assessing the overall fit of the linear regression model, the variables were found to significantly predict the subaxial muscle CSA/VBA ratios. Of the variables tested, female sex was independently associated with lower muscle CSA/VBA ratios for the SF, DF, and SE PSMs. A longer duration of symptoms and a steeper taper ratio were significantly associated with a lower DE CSA/VBA ratio, and the presence of neck pain was associated with a lower DF CSA/VBA ratio.

Interobserver Variability

The agreement between the observers for measurement of the PSM areas was substantial (weighted kappa coefficients: 0.71 for the suboccipital muscles, 0.78 for the subaxial muscles), and the agreement for the measurement of taper ratio and PFV/ICV was almost perfect (weighted kappa coefficients: 0.97 and 0.94, respectively).

Discussion

The natural history and pathophysiology of CMI remain unclear. Various clinoradiological phases in its pathophysiological continuum include a presyrinx state,⁶ syringomyelia,^{6,19} and scoliosis.¹⁹ The deleterious effect of CMI on cervical PSMs becomes obvious in the setting of scoliosis, the pathological end point of CMI. PSM atrophy at this stage is attributed to the effect of preceding syringomyelia on the anterior/posterior horn cells. The occurrence of scoliosis in the absence of preceding syringomy-

FIG. 5. Cervical canal taper ratio slope from C-1 to C-7 in patients with CMI (left) and in control subjects (right).

TABLE 2. Muscle areas in comparison group versus patients with and without neck pain

Muscle	Comparison Group (n = 25)*	Patients w/o Neck Pain (n = 13)*	p Value†	Patients w/ Neck Pain (n = 12)*	p Value†
RCmi CSA/OCA	0.65 ± 0.44	0.56 ± 0.22	0.49	0.60 ± 0.32	0.72
RCma CSA/VBA	0.49 ± 0.16	0.58 ± 0.20	0.13	0.60 ± 0.19	0.07
SF CSA/VBA	1.24 ± 0.50	1.16 ± 0.33	0.60	1.08 ± 0.16	0.28
DF CSA/VBA	0.42 ± 0.12	0.45 ± 0.17	0.53	0.34 ± 0.10	0.05
SE CSA/VBA	1.15 ± 0.40	1.13 ± 0.47	0.89	1.02 ± 0.30	0.32
DE CSA/VBA	0.93 ± 0.11	0.81 ± 0.18	0.01	0.79 ± 0.14	0.002
DF CSA/DE CSA	0.40 ± 0.12	0.50 ± 0.21	0.06	0.41 ± 0.21	0.85
SF CSA/SE CSA	1.11 ± 0.27	1.10 ± 0.32	0.91	1.05 ± 0.27	0.53

* Values are presented as the mean ± SD.

† p values are for t-test comparisons of the patient subgroups with the comparison group.

elia in CMI has been explained by asymmetrical tonsillar herniation and dorsal column compression²² contributing to a loss of spinal alignment and ensuing PSM weakness. Some studies have established reversibility of the PSM changes²³ and degree of scoliosis¹⁸ following surgical intervention in CMI. Given these facts, it is surprising that in a developmental disorder with so many PSM-related implications, there has been no study that has analyzed their morphometric alterations.

Alterations in PSMs in Other Conditions

PSM area and function have been studied in normal subjects and in various disorders. Age,¹⁵ bone mineral density,¹³ body mass index,³ hormonal influence,¹³ and physical training¹⁷ are some of the factors that have been demonstrated to alter PSM CSA or function. Conditions such as whiplash-associated disorders (WAD), cervicogenic headache,^{10,12} and cervical spondylotic myelopathy²¹ reportedly cause a dysfunction of the deep cervical flexors. Dysfunction of the deep cervical extensors has been documented in some studies on patients with WADs.^{1,2} Fatty infiltration in the suboccipital muscles has been noted in chronic neck pain,¹⁴ and selective dysfunction of the RCmi muscle has been implicated in chronic tension-type headache.⁵ The deep PSMs and the suboccipital muscles are predominantly composed of Type I fibers, with a high density of muscle spindles. Alteration of afferent input from these fibers explains the disturbances in proprioceptive function and kinesthetic sense in these disorders.¹⁴

Atrophy of PSMs in CMI

Compared with the normative control subjects, patients with CMI in our study demonstrated atrophy of the RCmi and all of the subaxial muscles. Generalized involvement of the cervical PSMs in a pathology at the CVJ could be attributed to neck pain–related disuse or fatty infiltration, dorsal column compression by the tonsils at the CVJ (alluded to earlier), or dysfunction of the anterior/posterior horn cells by altered CSF dynamics within the spinal cord. Although age did not affect the PSM areas, smaller areas of the flexors and SEs were more common in the female sex. Neck pain in the CMI subjects in our study correlated well with DF atrophy, a finding that is similar to that in other studies on chronic neck pain.

Implication of Cervical Myodural Bridges in CMI

Cervical myodural bridges are anatomical soft tissue bridges across the cervical epidural space that connect the suboccipital muscles to the dura mater.^{4,16} Postulated to play a role in monitoring dural tension, these bridges prevent dural buckling and maintain patency of the spinal canal.⁴ Alterations in their actions are of relevance in the setting of a crowded subarachnoid space in CMI. The RCma areas were found to be higher in our study cohort compared with the control subjects. This may be attributed to a compensatory hypertrophy in the setting of dysfunctional cervical myodural bridges. Our finding lends credence to the proposition that failure of the myodural bridges and

TABLE 3. Correlations between muscle area/bony area ratios and various factors

Muscle	Pearson's Correlate (p value)				
	Age	Duration of Symptoms	PFV/ICV	Tonsillar Herniation	Taper Ratio
RCmi CSA/OCA	0.17 (0.46)	−0.09 (0.70)	−0.06 (0.78)	0.12 (0.60)	0.01 (0.17)
RCma CSA/VBA	0.25 (0.25)	−0.06 (0.79)	−0.21 (0.33)	0.09 (0.70)	0.09 (0.68)
SF CSA/VBA	0.10 (0.63)	−0.27 (0.21)	−0.29 (0.19)	0.18 (0.43)	0.29 (0.18)
DF CSA/VBA	0.32 (0.14)	−0.32 (0.14)	−0.33 (0.13)	0.21 (0.35)	0.26 (0.22)
SE CSA/VBA	0.27 (0.21)	−0.36 (0.09)	−0.24 (0.27)	0.39 (0.07)	0.65 (0.001)
DE CSA/VBA	0.18 (0.43)	−0.54 (0.01)	−0.24 (0.28)	0.31 (0.16)	0.18 (0.41)
DF CSA/DE area	0.36 (0.09)	−0.04 (0.85)	−0.13 (0.55)	0.10 (0.65)	0.45 (0.03)
SF CSA/SE area	0.22 (0.30)	0.41 (0.05)	−0.01 (0.96)	0.34 (0.12)	−0.53 (0.009)

TABLE 4. Linear regression analysis

Variable	SF CSA/VBA			DF CSA/VBA			SE CSA/VBA			DE CSA/VBA			DF/DE			SF/SE		
	B	St E	p Value	B	St E	p Value	B	St E	p Value	B	St E	p Value	B	St E	p Value	B	St E	p Value
Age	0.02	0.01	0.97	0.78	0.00	0.09	0.08	0.01	0.79	0.46	0.01	0.32	0.12	0.01	0.82	-0.18	0.01	0.69
Sex	0.66	0.16	0.04	-0.63	0.07	0.03	-0.42	0.14	0.03	-0.06	0.11	0.82	-0.57	0.13	0.09	-0.05	0.15	0.86
Duration	-0.01	0.00	0.97	-0.15	0.00	0.51	-0.31	0.00	0.05	-0.30	0.00	0.04	0.15	0.00	0.58	0.65	0.00	0.05
PFV/ICV	-0.17	5.35	0.68	-0.72	2.44	0.06	0.12	4.59	0.62	-0.67	3.47	0.99	-0.04	4.13	0.91	-0.33	5.00	0.37
Cine (A)	0.15	0.21	0.69	-0.46	0.10	0.19	0.28	0.18	0.24	-0.25	0.14	0.48	-0.14	0.16	0.72	-0.16	0.20	0.65
Cine (P)	0.14	0.28	0.73	0.66	0.13	0.08	-0.14	0.24	0.57	0.80	0.18	0.05	-0.02	0.22	0.95	0.24	0.26	0.51
Tonsillar herniation	-0.15	0.01	0.62	-0.26	0.00	0.33	0.03	0.01	0.86	0.41	0.01	0.16	-0.58	0.01	0.85	-0.27	0.01	0.32
Taper ratio	0.03	0.21	0.94	-0.53	0.10	0.15	0.52	0.18	0.05	-0.92	0.14	0.03	0.43	0.16	0.32	-0.47	0.20	0.21
Neck pain	-0.55	0.23	0.21	-0.89	0.10	0.03	-0.27	0.19	0.28	-0.46	0.15	0.25	-0.39	0.18	0.38	-0.43	0.15	0.28

A = anterior; B = regression coefficient; P = posterior; St E = standard error.

Various subaxial muscle area/VBA ratios are the constants; various clinical and radiological factors are the variables.

the allied structures could result in altered CSF flow;⁴ this deserves further research.

Taper Ratio and Its Correlations With PSMs in CMI

It has been documented that the cervical spinal canal tapers mildly from rostral to caudal in healthy subjects.²⁰ A few studies have found this taper ratio to be greater in CMI^{7,8} and more so in patients with nondistended syringes²⁴ or scoliosis.⁷ The steeper tapering in CMI possibly results in higher CSF pressure gradients between the cranial and caudal ends of the spinal canal, resulting in dysfunctional CSF flow that favors the formation of a syrinx.^{7,8} It has been suggested that this bony variation in the cervical spine could be a component of the mesodermal derangement of CMI.²⁴ Our study has again demonstrated significantly steeper cervical taper ratios in patients with CMI compared with control subjects. Although bivariate analysis demonstrated that the taper ratio was correlated with other PSM areas, multiple regression analysis established that it was independently associated with atrophy only in the DEs, the muscles that were found to be the most affected.

Implications of the Study

Among all of the PSM changes seen in our study cohort, the alteration in the DEs was statistically significant. It remains to be seen whether changes in the remaining cervical PSMs in CMI gain significance in studies with larger sample sizes. The findings of particular interest in our study are the strong correlations of a longer duration of symptoms and steeper cervical taper ratios with DE atrophy. Given that WADs and alterations in cervical extensor muscles are closely associated, it is possible that a steeper cervical taper ratio and the accompanying abnormal cranial-caudal CSF gradients in patients with CMI predispose their spinal cords to a whiplash-like condition. Because a history of preceding trauma was not apparent in our patients, it is plausible that the whiplash-like condition was engendered by repeated and unnoticed microtrauma in their anomalous cervical spines. The morphometric altera-

tion in the DEs was demonstrable even without coexistent syringomyelia and became more pronounced over time.

In light of the above postulations, cervical mesodermal derangements in CMI may have a clinically significant predictive and prognostic value. Further research is warranted to confirm if PSM changes are demonstrable even in asymptomatic patients with CMI. A steep cervical taper ratio and/or PSM changes could then be additional indications for surgery in CMI, especially in the early part of its natural history when the role of surgery is controversial.

Limitations of the Study

The addition of a validated outcome measure for neck pain would have helped evaluate correlations of PSM areas with the degree of neck pain in CMI. Another limitation of our study is the unavailability of follow-up PSM CSA values, which would have provided information on their reversibility after surgery and correlations with postoperative clinical outcomes.

Conclusions

Patients with CMI demonstrate alterations in their cervical paraspinal musculature, even in the absence of coexistent syringomyelia. Their DE muscles undergo significant atrophic changes that worsen with the duration of their symptoms. This could be related to a significantly steeper cervical taper ratio that their cervical cords are exposed to. Neck pain in these patients is related to atrophy of their DF muscles. A steeper cervical taper ratio and alterations in the PSMs could be additional indicators for surgery in patients with CMI without syringomyelia.

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Disclosures

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

Author Contributions

Conception and design: Thakar, Kurudi Siddappa. Acquisition of data: Thakar, Kurudi Siddappa. Analysis and interpretation of data: Thakar, Aryan, Mohan, Sai Kiran. Drafting the article: Thakar, Aryan, Mohan. Critically revising the article: Thakar, Kurudi Siddappa, Aryan. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Thakar. Statistical analysis: Thakar. Study supervision: Hegde.

Correspondence

Sumit Thakar, Department of Neurological Sciences, Sri Sathya Sai Institute of Higher Medical Sciences, Bangalore 560066, India. email: sumit.thakar@gmail.com.