Chiari malformations associated with transverse myelitis: Are these myelopathies truly inflammatory?

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BACKGROUND

- Transverse myelitis (TM) is neuroinflammatory disease affecting the spinal cord
- Few cases are reported of myelopathy associated with Chiari malformation (CM). It is unclear whether these cases are inflammatory or non-inflammatory.
- Distinguishing these entities is important for clinical management and prognosis.

OBJECTIVE

We report a series of young patients with transverse myelitis associated with Chiari malformation.

METHODS

- Retrospective record review was performed of patients referred to the Johns Hopkins TM Center (JHTMC) from 2010 to 2017.
- Patients were included if they had a diagnosis of TM and CM.
- History, laboratory and imaging findings were extracted from the medical record.

RESULTS

- 86 patients ages 0 to 21 years seen at the JHTMC. Seven patients (8%) with TM and CM were identified. Six of seven (88%) were male.
- Five patients had onset between 4 and 10 months of age, one had onset at 3 years of age and one had onset at 21 years of age.
- All patients were previously healthy with no prior medical conditions. No patients reported any systemic or neurologic symptoms prior to onset suggestive of symptomatic CM.
- All patients presented with hyperacute onset of flaccid quadriplegia with median progression to nadir of 3 (range 2.0-17.0) hours. Of note, three of five infants presented acutely after awakening from sleep.

Table 1: Symptoms at Presentation of Patients with TM & CM

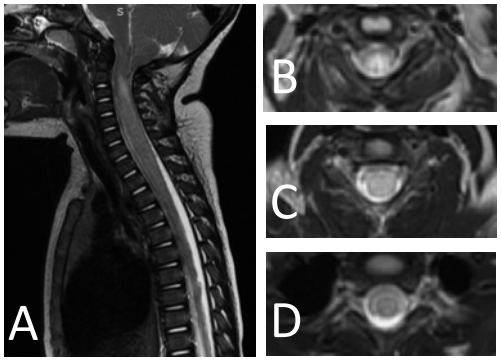
Flaccid Quadraplegia, n (%)	7 (100)
Sensory Changes, n (%)	1 (14)
Urinary Retention/Incontinence, n (%)	6 (88)
Respiratory Compromise, n (%)	2 (29)
Cranial Nerve Involvement, n (%)	0 (0)
Neck flaccidity, n (%)	3 (43)
Cognitive changes, n (%)	0 (0)

- Spinal cord MRI showed longitudinally extensive T2 hyperintensities in all patients, primarily affecting the gray matter of the cervical spine, extending as high as the medulla and as low as T6.
- Lesions were non enhancing in all cases.

Table 2: Imaging Findings in Patients with TM & CM

Patient	Spinal Cord Lesion	Tonsillar Herniation
1	C2-T2	8 mm
2	C2-C8	Present, mm not reported
3	C1-T6	4 mm
4	C2-T1	10 mm
5	C2- T1	5 mm
6	Medulla-T1	7 mm
7	C2-T5	8 mm

FIGURE 1: T2W MRI of a Patient #1, 8 month old male with flaccid quadraplegia showing (A) a longitudinally extensive hyperintense lesion extending from approximately C2 to T2 with associated edema of the cervical cord and herniation of the cerebellar tonsils into the foramen magnum. Corresponding axial images illustrate hyperintensities at the C2 (B), C5 (C), and T1 (D) levels.



- Further neuroimaging revealed diffusion restriction in the cord in one patient and asymmetry of the vertebral arteries in one patient.
- CM were diagnosed at onset in 6 patients and at follow up in 1 patient. All were classified as Type 1.
- Five of seven (71%) patients had lumbar puncture performed. In three, the CSF was normal. In one patient, lumbar puncture performed two days after initial presentation showed CSF pleocytosis (WBC 58) and elevated protein. One remaining patient had elevated protein only. In all patients infectious and immune workup was negative.
- All patients were treated with high dose IV corticosteroids and IVIg. Four patients were also treated with plasmapheresis.
- All demonstrated partial improvement to treatment but at median 18 months follow-up all had residual spastic paresis in one or more extremities. At follow-up, six of seven (88%) patients had paraplegia; five of seven (71%) had sensory levels.
- None of the patients had relapse of myelopathy.

CONCLUSIONS

- We report seven cases of hyperacute onset flaccid quadraparesis associated with longitudinally extensive cervical myelopathy and CM, Type 1.
- The prevalence of CM in our pediatric TM population, 8%, was eight times that of the prevalence of CM in the general pediatric population reported as 1% by Aitken et al. 2009 and 0.6-0.9% in other studies of the adult population.
- Hyperacute presentation, lack of inflammatory changes on neuroimaging or in spinal fluid, and similar localization of these lesions suggest a vascular etiology with myelopathy secondary to hypoperfusion of the spinal cord. Mechanical compression of the anterior spinal artery or posterior spinal arteries at the junction with the vertebral arteries secondary to CM is a potential mechanism
- Infants may be particularly vulnerable to hyperflexion or hyperextension of the neck as they are growing and developing rapidly.
- Clinicians should consider this phenomenon in the differential diagnosis of acute onset myelopathy in childhood.

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