Current Concepts in the Pathogenesis, Diagnosis, and Management of Type I Chiari Malformations

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ABSTRACT

Type 1 Chiari malformations (CMs) are a group of congenital or acquired disorders which include the abnormal presence of the cerebellar tonsils in the upper spinal canal, rather than the posterior fossa. The resulting anatomic abnormality causes crowding of the structures at the craniocervical junction and can impair the normal flow of cerebral spinal fluid (CSF) in this region. This impairment in CSF flow dynamics can led to the development of syringomyelia or hydrocephalus. Type 1 CMs have been associated with a wide array of symptoms resulting from either cerebellar and brainstem compression and distortion or disturbances in CSF dynamics, and can affect both children and adults. The clinical diagnosis may be difficult. Age usually matters in the clinical presentation, and in symptomatic patients, surgical intervention is usually required.

KEYWORDS: Chiari I Malformation, cerebrospinal fluid, hydrocephalus, syringomyelia

INTRODUCTION

Chiari malformations are a group of disorders defined by structural defects of the cerebellum, pons, fourth ventricle, and upper spinal cord in relation to the foramen magnum and the skull base. In 1891, Chiari was the first to describe and define hindbrain herniation, representing downward displacement of the cerebellum, fourth ventricle, and brainstem.[1] Type 1 CMs are characterized by herniation of the cerebellar tonsils through the foramen magnum into the upper spinal canal. The resulting compaction and crowding at the craniocervical junction can disrupt normal cerebrospinal fluid flow, produce the so-called "Valsalva-induced" headaches, and may lead to the formation of a spinal cord syrinx or hydrocephalus.[2]

Chiari malformations are still listed as a rare disease by the Office of Rare Diseases of the National Institutes of Health. The estimated prevalence in the United States of type 1 CMs is less than one percent with a slight female predominance.[2] Speer et al. have estimated that 215,000 Americans may harbor a type 1 CM.[3] However, the routine use of magnetic resonance imaging (MRI) has led to more frequent identification of this disorder and type 1 CMs can be seen incidentally in approximately 1% to 4% of patients undergoing brain or cervical spine magnetic MRI studies.[4]

Most cases of type 1 CM are sporadic. Type 1 CMs can be found in association with other conditions such as neurofibromatosis, idiopathic intracranial hypertension (IIH), tethered spinal cord, connective tissue disorders, craniosynostosis and skull base abnormalities, intracranial hypotension and cerebellar hypertrophy in polymicrogyria.[5] It is still not fully understood whether these co-existing conditions are mere coincidences or true co-morbidities. The precise natural history of this disorder remains unclear although patients generally have symptomatic progression. There have been a few published reports of spontaneous resolution of type 1 CMs but most symptomatic cases require surgical intervention.[5,6]

PATHOGENESIS

Most cases of type 1 CM are congenital. Skull base abnormalities are seen in approximately 50% of type 1 CM cases, (i.e., basilar invagination, retroflect odontoid, platybasia etc.).[7] Although the exact etiology is unknown, this condition is thought to be secondary to insufficiency of the paraxial mesoderm after neural tube closure with underdevelopment of the occipital somites.[7,8] Milorat and coworkers examined reconstructed CT and MRI images in 388 patients with classic type 1 CMs, and morphometric analysis revealed reductions in the posterior cranial size and volume.[9] In severe cases, downward herniation of the brainstem may occur and is sometimes referred to as a type 1.5 CM.[7] Despite evidence supporting a genetic contribution to type 1 CMs (i.e., twins, familial clusters, and co-segregation with known genetic syndromes), limited research has been conducted to identify the specific genetic factors involved.[8]

Acquired type 1 CMs can occur when there is a significant cerebral spinal fluid (CSF) pressure gradient across the craniocervical junction, i.e., CSF leakage or lumboperitoneal shunts can produce negative downward pressure gradients leading to the development of a type 1 CM. In addition, conditions associated with raised intracranial pressure, such as hydrocephalus and IIH, can promote downward pressure gradient. The association of CM1 with tethered cord has led to the "caudal traction theory."[6]

Syringomyelia is identified in 30-85% of patients.[5,10,11] There are many hydrodynamic theories to explain the formation of syringomyelia[11]. Abnormal and increased pulsatile

motion of the cerebellar tonsils ("tonsillar pistoning") can produce selective obstruction of CSF flow during systole. The increased systolic CSF waves are then transmitted to the spinal subarachnoid space and drive the CSF into the central canal of the spinal cord through engorged perivascular and interstitial spaces and lead to syrinx formation.[12,13]

DIAGNOSIS

The clinical findings vary dependent on the age at presentation. Occipital headache and neck pain are the most common symptoms in adults.[10] In infants, oropharyngeal dysfunction or sleep apnea and other cranial nerve findings, i.e., strabismus, are the most common presenting symptoms, while older children often present with headaches aggravated by " Valsalva maneuvers" during coughing and sneezing or strain, and scoliosis.[14,15] Symptoms are based on the structural and functional (impaired "CSF-dynamics") pathology associated with CM, which often leads to a wide spectrum of focal and non-focal findings in the clinical and neurological presentation, making it difficult to diagnose. Even more challenging is the often reported "brain fog" that has been largely attributed to chronic pain, depression and anxiety associated with the unknowns and physical challenges of this disorder. In traditional thinking, a disorder like Chiari affecting the craniocervical junction and the cerebellum, has not been thought to affect cognitive function: Altered MRI diffusion tensor imaging (DTI) metrics in the genu of the corpus callosum, splenium, fornix have been correlated with cognitive neurocognitive function in Chiari.[16]

Magnetic resonance imaging is the widely accepted diagnostic tool for type 1 CMs. The McRae line is a radiographic line drawn on a lateral midsagittal section of CT or MRI, joining the basion and opisthion representing the level of the foramen magnum. The traditional definition of type 1 CM as greater than 5 mm displacement of the cerebellar tonsils below the foramen magnum is challenged.[15] Even a "mild" displacement of 3-5 mm may be considered significant in the presence of neurological signs or symptoms or in the presence of syringomyelia. Also, the level of tonsillar ectopia evidenced in the sagittal MRI varies based on head position, and whether the measurement of the tonsillar position is based on a brain or spinal MRI. Recently, upright MRIs have challenged this view also, as gravity might reveal tonsillar displacement that was not seen in the traditional supine MRI versions.

The future lies in computation of the CSF space at the craniocervical junction and the resulting altered compliance and failure to synchronize transmission of systolic CSF pressures between the cranial and cervical subarachnoid space.[12]

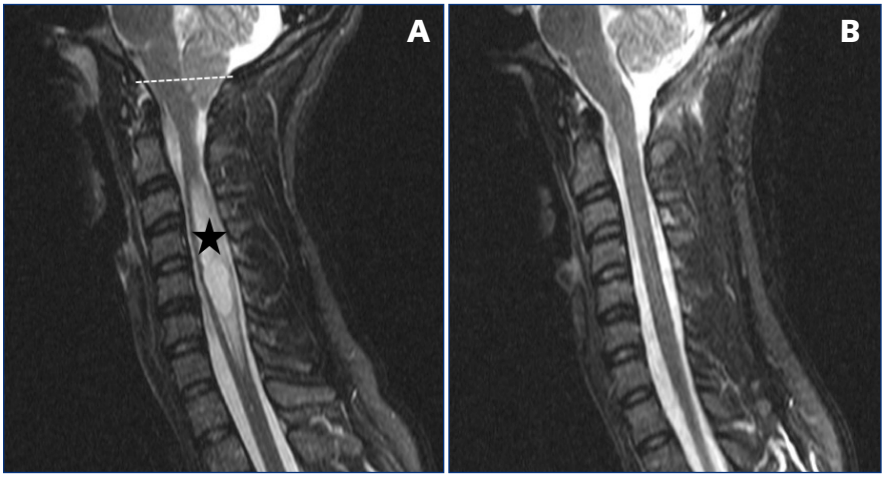
SURGICAL MANAGEMENT

The management of acquired forms of type 1 CM is directed at correcting the primary causative condition. For example, ventricular shunting for the treatment of hydrocephalus, repairing spinal CSF leakage, or correcting a tethered spinal cord usually results in anatomic and physiologic correction of the acquired CM. Intervention to directly treat the acquired CM is typically not necessary.

Asymptomatic patients who have an incidental finding on imaging are usually observed and monitored with follow-up MRI studies. Most patients with symptoms, or those who harbor a large associated spinal cord syrinx, should be recommended surgical intervention. Close follow-up and serial MRI imaging is required in patients who undergo observation alone in the presence of a syrinx. Appropriate management of an asymptomatic patient with a small syrinx is controversial.[17,18]

Many different surgical techniques are utilized to treat type 1 CMs, and there is no consensus. Surgical correction of type 1 CMs may include bony decompression of the posterior fossa with or without duraplasty, arachnoid dissection, or shrinking of the cerebellar tonsils. The goal of any of these operations is to restore adequate CSF flow at the level of the foramen magnum and establishment, basically an "anatomical reconstruction," of the Cisterna magna (**Figure 1A, B**). Bony decompression alone has been associated with a decreased risk of CSF related complications such as pseudomeningocele, meningitis, and hydrocephalus.

Figure 1. (**A**) Sagittal T2 STIR magnetic resonance imaging showing Chiari I with significant cervical syringomyelia (black asterisk) and the classical "crowding" of the cerebellum and the brain stem at the level of the foramen magnum (dashed white line equals the McRae line, which indicates the level of the foramen magnum on a midsagittal section of CT or MRI joining the basion and opisthion). (**B**) At 3 months follow-up, there is evidence of restored CSF signal anterior to the brain stem, decompression of the obex and restoration of the cisterna magna associated with an almost complete resolution of the syrinx.



However, multiple studies have shown that reoperation rates are higher for patients who have undergone bony decompression alone.[19,20,21] Duraplasty involves the use of autologous pericranium or allografts, none of which have been found superior to the other. More involved arachnoid dissection to ensure flow through native CSF channels may be required, particularly if scarring or webbing is restricting CSF flow. Shrinking of the cerebellar tonsils using meticulous bipolar cautery is also controversial, although we do advocate this approach in select cases. A recent meta-analysis suggested shrinking the cerebellar tonsils during the procedure showed better clinical results in patients with syringomyelia.[20] Shunting of an associated spinal cord syrinx has been largely abandoned. CM1.5 and associated skull base anomalies may require occipital-cervical fusion and instrumentation due to associated craniocervical instability.

FUTURE DIRECTIONS

All efforts need to be directed to identify potential subgroups of type 1 CMs. This will result in better diagnostic methods and treatment that will eventually be tailored to the individual anatomic and physiologic characteristics. This includes experimental and molecular studies to further our understanding of the genetics and pathophysiology of type 1 CMs. Also, MRI studies need to advance imaging to allow computation of cerebrospinal fluid space before and after surgery and provide a reliable "disease biomarkers." A large randomized, prospective study evaluating available surgical techniques is required to definitively determine the most successful and safest treatment options for type 1 CMs.

The Center for CSF Disorders of the Brain and Spine at the Warren Alpert Medical School of Brown University supports these endeavors, and has recently started exploring cognitive mechanisms in conditions such as hydrocephalus, CM and syringomyelia and optogenetic manipulation of choroid plexus cells to gain new insights into CSF physiology in collaboration with the Brown Institute for Brain Sciences and the Neuroscience Department. The annual CSF disorder symposium at the Brown medical school supports the interdisciplinary management of Chiari and related CSF disorders in collaboration with the Chiari and Syringomyelia Foundation (http://csfinfo.org/).

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