Chiari malformation I and autism spectrum disorder: an underrecognized coexistence

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OBJECT Patients with symptomatic Chiari malformation Type I (CM-I) frequently present with headaches, neck pain, difficulty swallowing, and balance disturbances. In children with autism spectrum disorder (ASD), diagnosing CM-I can be a challenging task. Moreover, even if symptomatic, some patients do not undergo further evaluation or management, as their presentations are attributed to autism and its myriad symptoms. Therefore, cranial MRI findings were reviewed after evaluating and treating patients with coexisting ASD and CM-I. In this paper, the authors report on 5 children with ASD and symptomatic CM-I, including their clinical presentation, imaging studies, management, and outcomes, and discuss the likely underrecognized coexistence of these conditions.

METHODS All pediatric patients with ASD and cranial MRI conducted for any reason in the period from 1999 to 2013 were considered for analysis. All cases with concomitant symptomatic CM-I were eligible for this retrospective analysis.

RESULTS One hundred twenty-five pediatric patients diagnosed with ASD had undergone MRI, and 9 of them had evidence of cerebellar tonsillar herniation. Five patients were symptomatic and underwent suboccipital craniectomy, a C-1 or a C-1 and C-2 laminectomy, and duraplasty with bovine pericardium or Type I collagen allograft. There were no intraoperative complications. All patients showed symptom improvement and/or resolution of presenting symptoms, which included headache, dysphasia, speech, and irritability.

CONCLUSIONS There is no identified cause of autism. Children with ASD can be difficult to assess specifically in a neurological examination. Thus, cranial MRI considered when completing a comprehensive diagnostic evaluation. While cranial MRI is not a routine part of ASD evaluation, this study demonstrates that CM-I and ASD may coexist and be underrecognized. The study reinforces the importance of a comprehensive medical evaluation designed to elucidate neurological findings in children with impaired communication abilities and suggests the judicious use of neuroimaging.

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KEY WORDS Chiari malformation I; autism; autism spectrum disorder; suboccipital craniectomy

In 1891, Hans Chiari documented 3 cases of congenital defects of the rhombencephalon, classified as types I, II, and III.5 A Chiari I malformation, or Chiari malformation Type I (CM-I), is the mildest form and is associated with ectopia of the cerebellar tonsils through the foramen magnum, which can occur to various degrees. Diagnosis of CM-I is currently best made on cranial midsagittal MRI studies, with cerebellar tonsil herniation of at least 3 mm suggesting the condition.6

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by impairments in social interaction, communication difficulties, and the presence of restricted, repetitive, and stereotyped patterns of behavior. The disorder occurs in all ethnic, socioeconomic, and age groups. There is significant variability in terms of specific characteristics and severity.4,9,23 Frequently, impairments are readily apparent externally and consequently detract from other comorbidities, thereby making their diagnosis or treatment difficult.

In this report, we describe the presentation of symptomatic CM-I in five children with a preexisting diagnosis of autism and evaluate their imaging studies, management, and outcomes. The observation of CM-I in patients with ASD highlights the importance of considering CM-I in the ASD subset, especially when CM-I is symptomatic, and alludes to the likely undiagnosed and undertreated incidence that may exist. To our knowledge, no similar case series has been published thus far.

ABBREVIATIONS ASD = autism spectrum disorder; CM-I = Chiari malformation Type I.


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Methods

Institutional review board approval was obtained for this retrospective study of all patients younger than 18 years of age, who had a diagnosis of ASD and had undergone cranial MRI for various reasons over 13.5 years (1999–2013). All patients met the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (299.00) criteria for ASD. In addition, patients were assessed using the Autism Diagnostic Observation Schedule (ADOS), Autism Diagnostic Interview (ADI), Child Behavior Checklist (CBCL), Teachers Report Form (TRF), or the Pediatric Quality of Life Inventory (PedsQL). We sought all cases of ASD and concomitant symptomatic CM-I. Symptoms were based on reports from parents, pediatricians, pediatric neurologists, and school teachers.

Results

From an institutional database of 125 patients, 9 (7%) had evidence of cerebellar tonsillar herniation, which included cerebellar ectopia and CM-I. Symptomatic CM-I was defined as difficulties with balance, swallowing, or mood or subjective findings of headache. Five patients were symptomatic, and the details of each case are outlined below. The other four patients were asymptomatic and had cerebellar ectopia of less than 4 mm. Table 1 summarizes the extent of cerebellar ectopia in the patients in our series. All patients underwent a suboccipital craniectomy, a C-1 or a C-1 and C-2 laminectomy, and duraplasty with bovine pericardium or Type I collagen allograft. Intraoperatively, extensive arachnoid adhesions were present around the cerebellar tonsils and foramen magnum, requiring lysis to obtain adequate decompression and restore normal CSF flow (if compromised). There were no intraoperative or postoperative complications. All patients showed symptom improvement following surgical intervention. Presenting symptoms varied among the cases. The following improvements were recorded: 100% headache resolution (4 of 4 patients), 75% improvement in dysphagia (3 of 4), 50% improvement in speech (2 of 4), improvement in cervical range (1 of 1), reduced syrinx size (1 of 1), and improved cognitive function (1 of 1).

Illustrative Cases

Case 1

History and Examination

A 4-year-old boy with a history of autism and generalized seizure disorder presented for evaluation. Autism had been diagnosed when he was 18 months of age because he demonstrated impaired social function, lack of visual contact, sensory interrogation difficulties, and marked speech delay. Electroencephalography demonstrated no lateralizing findings, and his generalized seizure disorder was well controlled by Keppra (levetiracetam). His parents had observed that he frequently held his head and would bang it on walls. He additionally had difficulty swallowing and was nonverbal. Physical examination revealed bilateral, symmetrical hyporeflexia (1+) and difficulties with balance upon ambulation. Direct evaluation of the lower cranial nerves was not possible because of patient noncompliance.

Imaging

Magnetic resonance imaging of the brain (Fig. 1 left) was performed primarily to evaluate the seizure disorder. A follow-up MRI study of the brain together with a CSF flow study demonstrated evidence of 19 mm of cerebellar tonsil herniation and moderate to severe impairment of CSF flow in the posterior fossa. No hydrocephalus or parenchymal abnormality was visualized.

Postoperative Course

The patient underwent the surgical procedure described above. Follow-ups at 1, 3, and 12 months after surgery revealed progressive improvement in balance along with the resolution of his swallowing difficulties. In addition, normal cervical flexion and extension returned, with no complaints of headache or neck pain. The boy’s seizures continued to be well controlled by the Keppra. An MRI study at 1 year postoperatively revealed decompression of the CM-I with reduction in the syrinx size (Fig. 1 right).

Case 2

History and Examination

A 4-year-old boy with a history of autism, which had been diagnosed when he was 18 months, and a possible absence seizure–like episode presented to his neurologist. Electroencephalography was normal. An MRI study of the brain revealed CM-I, and consequently he was referred for further evaluation. His parents also revealed that he frequently held his head and would bang it on walls. He additionally had difficulty swallowing and was nonverbal. Physical examination was difficult to complete because of patient noncompliance, although he appeared to be very active and ambulatory with occasional balance difficulties.

Imaging

An MRI study of the brain demonstrated 8 mm of cerebellar herniation without parenchymal abnormalities or hydrocephalus.

Postoperative Course

The patient underwent the surgery. At 1 and 6 months

TABLE 1. Pathological MRI findings of 9 patients with concomitant ASD and CM

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Amount of Cerebellar Ectopia (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic (n = 5)</td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>19</td>
</tr>
<tr>
<td>Case 2</td>
<td>8</td>
</tr>
<tr>
<td>Case 3</td>
<td>8</td>
</tr>
<tr>
<td>Case 4</td>
<td>13</td>
</tr>
<tr>
<td>Case 5</td>
<td>8</td>
</tr>
<tr>
<td>Asymptomatic (n = 4)</td>
<td>&lt;4</td>
</tr>
</tbody>
</table>

N = number of patients.
postoperatively, the boy demonstrated improvement in his balance, irritability, and mood as well as his swallowing capabilities. In addition, he had ceased banging his head on the wall and was easier to reason with. He continued to remain largely nonverbal but would occasionally speak a few words. An MRI study was not obtained postoperatively.

Case 3
History and Examination
A 4-year-old boy presented to the clinic for evaluation. Autism had been diagnosed when he was 15 months of age. He had a history of head holding, banging his head on the wall, throwing frequent tantrums, and biting his hands. Additionally, he had difficulty swallowing food as well as excessive regurgitation of fluids. At 2 years of age, he had been diagnosed with metopic craniosynostosis, for which he underwent cranial vault remodeling without complication. Magnetic resonance imaging at the time had demonstrated a 6-mm CM-I, for which he did not receive treatment. His symptoms had reduced immediately following the cranial vault remodeling but recurred and worsened over the ensuing 2 years. Physical examination could not be completed because he was noncompliant, although he was ambulatory without difficulty and nonverbal.

Imaging
An MRI study of the brain with a CSF flow study was performed. Compared with the MRI results from 2 years earlier, an increase in the cerebellar tonsil herniation to 8 mm had occurred. In addition, CSF flow was reduced in the posterior fossa. There was no hydrocephalus, and there were no parenchymal abnormalities. The calvaria demonstrated appropriate surgical correction.

Postoperative Course
The patient underwent surgical treatment. At 1 and 9 months postoperatively, he demonstrated continued improvement in socializing and function. He had ceased banging his head, rarely had a tantrum, and was starting to verbalize with apparent improvement in understanding. Follow-up MRI is scheduled.

Case 4
History and Examination
A 5-year-old boy presented to the clinic after being referred for symptoms suggestive of headaches based on his parents’ observation. He had a concurrent diagnosis of autism with severe delay in speech function. Physical examination was normal with the exception of the severe speech development delay.

Imaging
An MRI study of the brain with a CSF flow study was performed. It demonstrated a CM-I with 13 mm of cerebellar tonsil herniation as well as severe restriction of CSF flow in the posterior fossa. There was no hydrocephalus or parenchymal abnormality.

Postoperative Course
The patient underwent surgery. At his last visit, 2 years postoperatively, his parents no longer observed him having features suggestive of headaches. He continued to have speech difficulties. Magnetic resonance imaging performed at the time demonstrated good posterior fossa decompression without evidence of CSF flow restriction.

Case 5
History and Examination
A girl with an age of 3 years 9 months presented to the clinic after having been referred for a CM-I. Autism had been diagnosed when she was 16 months old, and she had significant speech delay with poor social interaction. She also had balance difficulties and would choke on food and bang her head on the wall. Physical examination was not completed because of patient noncompliance, although she was observed to be nonverbal with occasional balance difficulties while ambulating.

Imaging
Magnetic resonance imaging of the brain with a CSF flow study demonstrated 8 mm of cerebellar tonsil herniation. There was moderate to severe CSF flow restriction in the posterior fossa. There was no hydrocephalus or parenchymal abnormality.

Postoperative Course
At 1, 6, and 12 months postoperatively, the patient demonstrated improved swallowing and speech with no episodes of head banging. In addition, her balance had normalized. An MRI study performed at the time demonstrated good posterior fossa decompression and no evidence of CSF flow restriction in the posterior fossa.

Discussion
Chiari malformation I is frequently asymptomatic,12 and consequently its true prevalence is unknown. A symptomatic CM-I can cause neurological dysfunction either by direct compression of neural tissue with or without syringomyelia, or as a consequence of CSF circulatory disturbances. Consequently, the most frequent presenting features include headaches, ocular disturbances, sleep apnea, lower cranial nerve compression, dysphagia, dysar-
Thria, disequilibrium with vertigo, and motor or sensory findings caused by syringomyelia or scoliosis.\(^1\)\(^2\)\(^3\)

There is evidence to suggest that CM-I can negatively affect higher cognitive functioning and development,\(^4\)\(^5\)\(^6\) although the exact etiology and pathogenesis remain controversial. Regarding the development of CM-I, various hypotheses have been proposed, including primary genetic abnormalities,\(^7\)\(^8\)\(^9\) early gestational injuries, and postnatal osseous growth abnormalities.\(^10\)\(^11\)

It is well known that ASD is characterized by significant impairment in interest, social development, and communication and an increase in repetitive and stereotypic behaviors.\(^12\)\(^13\)\(^14\) Children with ASD have considerable difficulty communicating emotions and discomfort. Genes that may be involved in the development of ASD and CM-I have been individually identified,\(^15\)\(^16\) yet the incidence and prevalence of these disorders simultaneously in the same patient have not been characterized. Functional MRI abnormalities of the amygdala, cerebellum, orbitofrontal cortex, and superior temporal gyrus have also been found to be associated with ASD.\(^17\)\(^18\) Yet, it is unlikely that these anatomical abnormalities alone are responsible for CM-I in this patient subset, as both disorders exist independent of each other. More than likely, a certain subset of patients with ASD has other developmental abnormalities that result in CM-I, with a further subset becoming symptomatic.

Because of the young age and clinical heterogeneity of patients with ASD, it can be extremely difficult to identify coexisting symptomatic CM-I. Features such as head holding, head banging, and difficulty in flexion and extension of the neck suggest the likelihood of headaches and neck pain. Swallowing difficulties and dysarthria may lower cranial nerve dysfunction, while difficulties in balance and ambulation may reflect cerebellar or spinal cord compromise.

Unfortunately, these clinical features are frequently thought to be caused by ASD and consequently are not investigated further. This, in turn, places an additional burden on patients and their families, as a timely diagnosis with appropriate treatment can reduce these comorbidities and improve patients’ quality of life. It is likely that there are an underdiagnosed and undertreated number of patients with these two conditions simultaneously. The current frequency of CM-I in the pediatric and adult population is thought to be about 1%–3.6%.\(^1\)\(^9\)\(^19\)\(^20\) This rate is lower than the observed frequency of 7% in our population database.

Nevertheless, it is difficult to recommend performing cranial imaging in all patients with ASD to evaluate for CM-I, as the patient may be asymptomatic and such a practice does not represent a cost-effective form of health care delivery. Currently, the American Academy of Neurology, the Child Neurology Society,\(^2\) the American Academy of Child and Adolescent Psychiatry,\(^2\) and the American Academy of Pediatrics\(^8\) do not recommend imaging as part of the routine evaluation of children with ASD.

It is therefore imperative that the physician is alert to the history given by the child’s parents or caretakers, as well as the observed clinical findings, and corroborates these aspects with the sensible utilization of further testing and subsequent management. Awareness of the coexistence of symptomatic CM-I and ASD necessitates clear communication between primary care physicians, autism specialists, pediatric neurologists, and pediatric neurosurgeons.

**Conclusions**

We identified and treated 5 patients with symptomatic CM-I with ASD from a well-characterized sample. All patients tolerated the surgical intervention and showed improvement in their baseline symptoms including subjective headache, dysphagia, and speech difficulty. While our sample is small, it represents an opportunity for further investigation into the coexistence of ASD and CM-I. A larger population database must be reviewed to establish whether the frequency of CM-I is indeed higher in those with ASD than in the general population.

**References**


Author Contributions
Conception and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Study supervision: Tanaka, Jayarao.

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