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Brain and Spine

Assessment of patients with a Chiari malformation type I

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ABSTRACT

Introduction: The prevalence of Chiari malformation type I (CM-I) has been estimated as up to 1% of the general population. The majority of patients are asymptomatic and usually do not need treatment. Symptomatic patients, and some asymptomatic patients with associated conditions, may benefit from further assessment and treatment.
Research question: The aim of this review was to describe the clinical and radiological assessment of patients presenting with a CM-I.
Material and methods: A literature search was performed using the PubMed and Embase databases focused on clinical assessment and imaging techniques used to diagnose CM-I.
Results: Following a complete clinical evaluation in patients with symptomatic CM-I and/or radiologically significant CM-I (tonsillar impaction, resulting tonsillar asymmetry and loss of CSF spaces), MRI of the brain and whole spine enables an assessment of the CM-I and potential associated or causative conditions. These include hydrocephalus, syringomyelia, spinal dysraphism, and tethered cord. Flow and Cine MRI can provide information on CSF dynamics at the craniocervical junction, and help in surgical decision-making. Hypermobility or instability at the upper cervical and craniocervical junction is less common and can be measured with CT imaging and flexion/extension or upright MRI.
Discussion and conclusion: The majority of CM-I detected are incidental findings on MRI imaging of brain or spine, and do not require intervention. Once a radiological diagnosis and concern has been raised, clinical assessment by an appropriate specialist is required. A MRI brain and cervical spine is indicated in all radiologically labelled CM-I. In symptomatic patients or cases of radiologically significant CM-I, MRI of the brain and entire spine is indicated. Further investigations should be tailored to individuals' needs.

1. Introduction

Originally described by the Austrian pathologist Hans Chiari in 1891, Chiari malformations (CMs) are hindbrain malformations that vary in severity (Chiari, 1895). According to the Chiari classification system, type I – III CM are graded based upon an increasing degree of hindbrain herniation through the foramen magnum. Type IV CM represents cerebellar aplasia or hypoplasia (Hadley, 2002). Recently type 0 and 1.5 CM have also been proposed, with type 0 CM describing a patient with symptoms and a syrinx, with '0 mm' of tonsillar descent, and type 1.5 referring to tonsillar herniation with additional caudal descent of the brainstem (Mariwalla et al., 2014). The term Complex Chiari has been used to describe cerebellar tonsillar herniation with another radiographic feature, such as a syrinx, medullary kink, cranial skull base abnormality, caudal descent of the brainstem, basilar invagination, or scoliosis (Brockmeyer, 2011).

Traditionally, the defining feature of the Chiari malformation type I (CM-I) is tonsillar descent of 5 mm or more beyond the foramen magnum (Elster and Chen, 1992). This definition is being questioned, as a more encompassing definition of symptomatic syndromes due to cerebrospinal fluid (CSF) obstruction, or compression at the craniocervical juction appears preferable, but no agreement has been reached, and the 5 mm rule is still used by most authors. Neuroradiology is essential in the diagnosis of CM-I to assess the anatomical structures and fluid dynamics that are associated with a CM-I. Magnetic resonance imaging (MRI), including dynamic and upright views, are described, as well as myelography and computed tomography (CT).

With the increasing use of neuroimaging, the number of 'victims of modern imaging technology' is on the rise (Hayward, 2003). More than 1% of the population are being diagnosed with CM-I, yet the vast majority of CM-I detected are incidental, and do not require treatment (Meadows et al., 2000; Langridge et al., 2017). A new diagnosis of a Chiari malformation can produce anxiety in patients, and be used to explain a myriad of symptoms, many of which are not improved with surgical 'correction'. The degree of tonsillar herniation alone does not correlate to its clinical significance, nor measure a functional deficit. The authors provide a review of the assessment for patients with a CM-I, including the newer radiological techniques that are increasingly being used.

1.1. Methods

A literature search was performed by two independent reviewers using PubMed and Embase databases focused on the clinical and radiological assessment used to diagnose CM-I. The following combined search terms: 'Chiari AND clinical', 'Chiari AND MRI', Chiari AND CT', 'Chiari AND syringomyelia', 'Chiari AND basilar invagination' and 'Chiari AND tethered cord' were used. To further identify all potentially relevant studies, we manually searched reference lists from all the retrieved articles. No time limit was set during the search. Indexes were last accessed on October 26, 2021.

1.2. Study criteria

The inclusion criteria were as follows: articles that addressed clinical presentation and investigation for CM-I, and articles that evaluated CM-I associated conditions. All publications were limited to human subjects and written in English.

2. Results

2.1. Search results

The search strategy identified 2854 articles. After removing duplicate studies, our inclusion and exclusion criteria were applied to the titles of the remaining articles, yielding 64 articles.

Ten studies described clinical presentations and physical examination findings in CM-I patients and associated conditions. Three articles evaluated the use of plain films and computed tomography as the screening tool for scoliosis and initial diagnostic tool for CM-I respectively. Twenty-six articles demonstrated the use of magnetic resonance imaging of the brain, which described the correlation between tonsillar herniation, tonsillar configuration, size of posterior cranial fossa, hydrocephalus and CM-I. Twenty-three articles discussed the use of dynamic flow and motility studies to assess CM-I symptoms, predict post-operative outcomes, as well as hypermobility syndromes. Nine articles evaluated the use of MRI of the spine to assess syringomyelia and tethered cord syndrome.

2.2. Discussion

2.2.1. Clinical assessment

The first part of any assessment is to take a clinical history and perform a complete physical and neurological examination (Fig. 1). The examination should include an assessment of hypermobility (Malfait et al., 2017). The classic symptom of CM-I is a severe transient sub-occipital headache, which is commonly aggravated by head dependency, postural changes, exertion, and the Valsalva maneuver (Mea et al., 2011). The pain may be caused by stretch of pain receptors at the foramen magnum, or a transient increase in pressure, although the true mechanism is not known. Chronic daily headache is common in CM-I patients, as in the general population (Taylor and Larkins, 2002). Otoneurological symptoms such as vertigo, nystagmus and tinnitus have been suggested to be due to cranial nerve traction from hindbrain descent (Mea et al.,

2011). Bulbar and other brain stem dysfunction, such as vocal cord paralysis, hoarseness, palatal weakness, tongue atrophy, cricopharyngeal achalasia, sleep apnoea and nystagmus, are rare in CM-I patients, but more common in patients with associated skull base anomalies, and may be due to compression of the lower cranial nerves and medulla (Dyste et al., 1989; Li et al., 2005). Peripheral neurological examination may find signs of an associated syrinx (Cahan and Bentson, 1982).

Syringomyelia can cause a progressive dissociated sensory loss, with spinothalamic pain and temperature pathways affected more than the dorsal column's light touch and proprioception, which spread in a cape-like distribution (Honan and Williams, 1993; Grant et al., 1987). Other symptoms and signs include weakness, initially in the intrinsic hand muscles, burning dysesthesia, autonomic dysfunction, spasticity, and scoliosis. Autonomic dysautomnia, chronic tiredness, and postural tachycardia syndrome have all been ascribed to excessive stretching or compression of the brain stem in patients with hypermobility at the craniocervical junction, although evidence supporting this view remains controversial (Henderson et al., 2017). Bladder and bowel dysfunction, back and leg pain, and leg weakness can be an indication of a tethered cord. Finally, an external examination for dysraphic signs including midline posterior dimples or hair tufts should be performed. After the history and examination, an assessment is made of the likelihood of the symptoms being related to the CM-I and/or associated conditions, their severity, and the potential need for, and benefit from, treatment.

The clinical and radiological assessment should take into consideration the underlying cause, as investigation and treatment should be directed at the cause rather than the resultant CM-I. An assessment of more than 700 patients with CM-I showed a variety of causes, and provides some guiding principles (Milhorat et al., 2010a). The commonest was a small posterior fossa (less than 190 mL). Other causes included increased pressure from above due to hydrocephalus, idiopathic intracranial hypertension, or a mass lesion, or something pulling from below, such as a tethered cord or reduced spinal subarachnoid pressure due to a lumbar peritoneal shunt or chronic CSF leak. The final associated cause was a base of skull and upper cervical spine abnormalities that could be structural or due to hypermobility.

2.3. Imaging evaluation

2.3.1. Plain films
Plain films are not generally used in the work up of patients with a CM-I, other than those with scoliosis. In children, up to 30% with a symptomatic Chiari and syrinx will develop scoliosis. The scholiosis in more than 50% of these children may be improved with treatment of their CM-I (Hwang et al., 2012). Plain X-rays of the entire spine are still used to assess, measure, and monitor the curve (Oestreich et al., 1998).

2.3.2. Computed tomography (CT)
With the ready availability and widespread use of advanced neuroimaging modalities, many patients are still initially diagnosed based on a CT scan. Whilst most patients will proceed to MRI, CT remains essential in assessing the bony anatomy in patients with congenital or acquired bony abnormalities at the craniocervical junction, and may help with dynamic examination (see dynamic mobility studies below). Basiler invagination, platybasia, klippel feil, atlanto occipital assimilation, and other more complex anomalies may be seen (Elster and Chen, 1992). CT may also be used in CT myelography for the assessment of occult spinal CSF leaks. Whilst MR myelography may be more accurate concerns remain about the use of intrathecal gadolinium (Chazen et al., 2014).

2.4. Magnetic resonance imaging (MRI) - brain

2.4.1. Tonsillar herniation
MRI of the brain and cervical spine remains the imaging modality of choice for the initial evaluation of CM-I. Traditionally, a radiological diagnosis of CM-I is made on the T1 or T2 sagittal midline view by
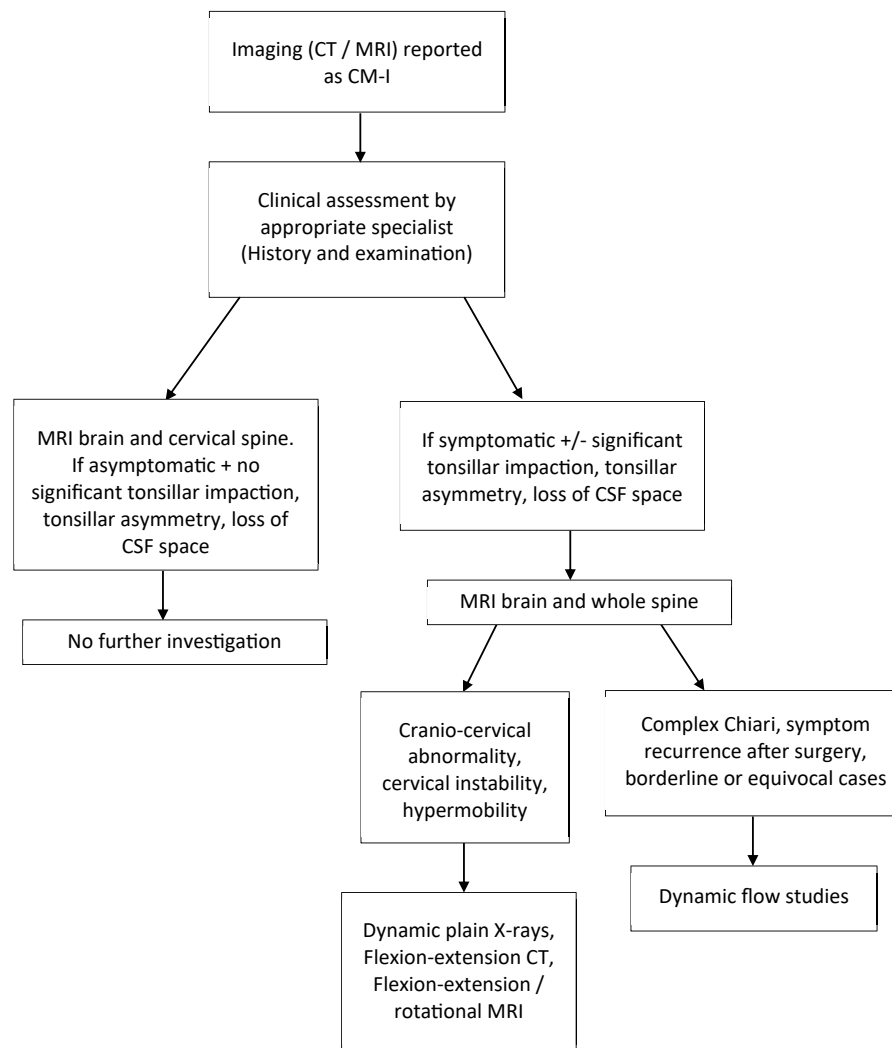
Fig. 1. Diagnostic flowchart of Chiari malformation.

measuring the perpendicular distance between the tip of the herniated tonsil and the foramen magnum (McRae's line). However, the tonsils exist in three dimensions, and can be unequal in size, shape, and projection. As such, coronal cuts may provide additional valuable information relating both to diagnosis and helping plan the surgical approach (Spinos et al., 1985).

Grading systems have been proposed, based on the degree of tonsillar herniation and the age of the patient. One group of authors suggested that the tonsils should be considered normal up to 3 mm, borderline between 3 and 5 mm, and pathologic when they exceed 5 mm (Aboulezz et al., 1985). Two further reports suggested age dependant cut off values of 6 mm up to 10 years, 5 mm 10–30 years, 4 mm 30–70 years, and 3 mm over 70 years (Smith et al., 2013; Mikulis et al., 1992). The ascent of the cerebellar tonsils with advancing age may have more to do with the gradual reduction in cerebral volume over time, rather than anything inherent in the CM-I itself.

As an absolute value, the number of mm of tonsillar descent is relatively unhelpful (Jussila et al., 2021), unless it is progressive which suggests increasing intracranial pressure or an ongoing pull from chronic spinal subarachnoid hypotension. Chiari 0 and Chiari 0.5 have been described, with patients with 0 mm or <5 mm respectively of tonsillar descent, with appropriate symptoms and improvement after surgery. The most important aspect of any radiological imaging is a clear assessment of the three-dimensional anatomy and CSF dynamics at the craniocervical junction.

2.5. Tonsillar configuration

The degree of tonsillar herniation has a poor correlation with the severity of symptoms, as up to 30% of patients with significant tonsillar herniation are asymptomatic (Elster and Chen, 1992). Instead, tonsillar shape has been used (Spinos et al., 1985; Meadows et al., 2000). Severe compression produces peg-like tonsils, which may further restrict CSF flow. Pegged tonsils are more common in patients with herniation >5 mm (85%) compared to rounded or intermediate shapes (Smith et al., 2013) (Fig. 2).

2.6. The size of posterior cranial fossa (PCF)

The commonest cause of a CM-I is thought to be an abnormality of the paraxial mesoderm, resulting in a developmental mismatch between the neural and bony structures (Milhorat et al., 1999). The size of the PCF can be measured using linear markers. The lengths of the clivus, supra-occiput, and exocciput are often shorter in patients with CM-I compared with healthy individuals, although the normal measurements can vary significantly (Milhorat et al., 1999; Nishikawa et al., 1997; Karagöz et al., 2002). One group proposed that occipital bone hypoplasia and reduced PCF volume, with no aetiological co-factors, were called classical CM-I (Milhorat et al., 2010a) (Fig. 3). Using measurements of the osseous PCF area, the clival length, the distance between the corpus callosum, pons, and the FM, a second group produced a probability model to
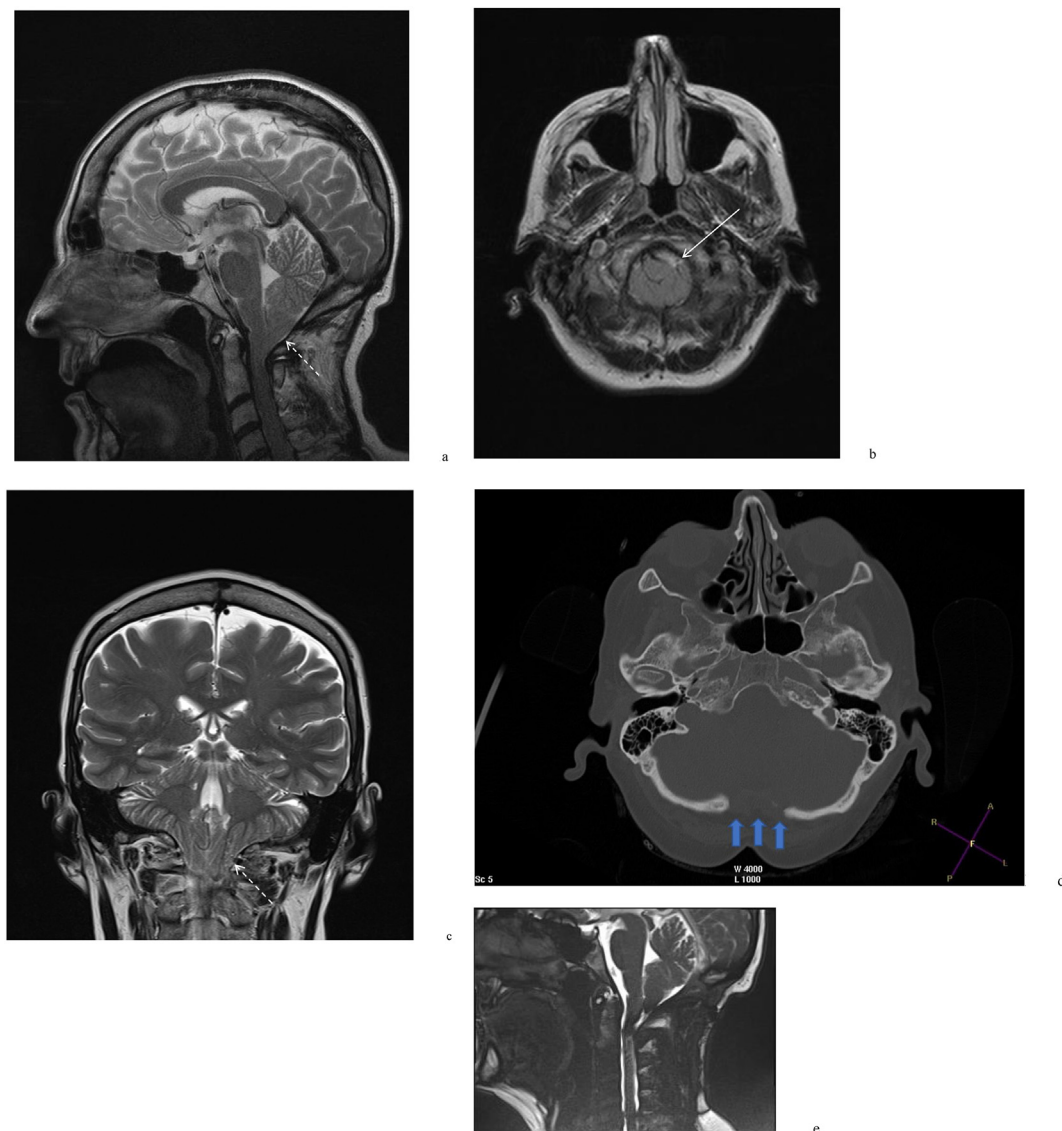
Fig. 2. Sagittal (a), axial (b) and coronal (c) T2 weighted images from a brain MRI demonstrating crowding of the CSF spaces at the level of the foramen magnum (solid white arrow) and a peg-like deformity of the cerebellar tonsils (white dashed arrow). A decompressive posterior fossa craniectomy (blue arrows) was performed (d) with CSF flow voids along the craniocervical junction anteriorly and posteriorly which appear as areas of darker signal (e). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

predict CM-I symptomatology regardless of the degree of tonsillar herniation with 93% sensitivity and 92% specificity (Urbizu et al., 2014). Similar morphometric findings were observed in patients with Chiari-like symptomatology without significant cerebellar tonsillar herniation (Sekula et al., 2005; Dufton et al., 2011). However, others have found no association between the size of PCF and clinical symptomatology (Stovner et al., 1993). Due to the lack of agreement between studies, at present, linear measurements of the posterior fossa do not appear to provide any additional information in radiological assessment.

There has been interest in investigating volumetric approaches. The posterior fossa volume is about 190 mL in normal individuals (Milhorat et al., 2010b). A volume ratio (brain volume divided by cranial volume in the PCF) to measure crowding was investigated and was significantly larger in CM-I when compared to that of healthy individuals (Nishikawa et al., 1997). Furthermore, a smaller ratio of PCF to supratentorial volume correlated to a better post-operative clinical outcome, as did the extent of the craniectomy and the degree of PCF volume increase (Badie et al., 1995). The optimal PCF volume increase and extent of craniectomy required could then be predicted on the basis of the pre-operative MRI

(Noudel et al., 2011). Despite these potential diagnostic and predictive benefits, PCF volume assessments are rarely used in clinical practice due to the laborious process of volume calculation, but may become useful as automatic segmentation algorithms improve.

2.7. Hydrocephalus

Chiari believed that CM were secondary to long standing hydrocephalus, although hydrocephalus and idiopathic intracranial hypertension (IIH) are seen in only 7–11% of patients with CM-I (Milhorat et al., 1999; Tubbs et al., 2003). A causal relationship may be different in different patients. It may be that occlusion of the foramen of Magendie and an associated CM-I obstruct IVth ventricle outflow leading to hydrocephalus, or that hydrocephalus or IIH leads to the downward herniation of the tonsils causing a CM-I (Orakdogen et al., 2015; Decq et al., 2001). As part of the initial clinical assessment of the patient, symptoms and signs of hydrocephalus are examined for, and if found, treatment should be directed at the hydrocephalus rather than the CM-I in the first instance (Hayhurst et al., 2008). MRI brain, MR or CT venography,
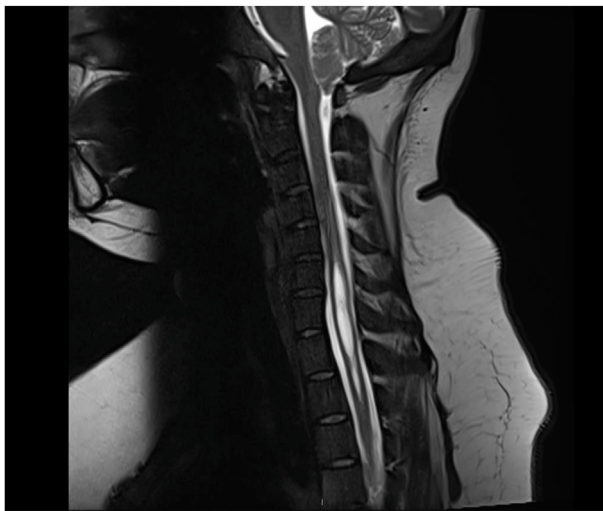
Fig. 3. Different causes of tonsillar descent. I. Small posterior fossa. Sagittal T2 weighted C-spine MRI of a patient pre (a) and post (b) posterior fossa decompression with a patch due, showing the early reduction in syrinx size following enlargement of the posterior fossa, and tonsillar cautery.

intracranial pressure monitoring, and venous pressure measurements can help establish treatment options.

2.8. Magnetic resonance imaging (MRI) – craniocervical junction – dynamic evaluation

2.8.1. Dynamic flow studies

Dynamic studies have been used to assess CM-I symptoms and predict post-operative outcomes. In normal individuals, CSF at the craniocervical junction flows in a pulsatile cranial, then caudal motion synchronized with cardiac and respiratory induced changes in intracranial blood volume (Wilson, 2016). The spinal arachnoid space acts as a buffer to limit intracranial pressure peaks (Whedon and Glassey, 2009). In children, greater intracranial compliance results in the faster caudal velocity (Ohara et al., 1988). Phase contrast cine MRI in symptomatic CM-I patients has identified greater fluctuations of CSF velocity in different regions, with a higher peak velocity at the FM (4.8 cm/s vs 3.3 cm/s in healthy controls), and a reduction in overall volume movement (Haughton et al., 2003; Quigley et al., 2004; Armonda et al., 1994). Flow jets are described, with regions with a preponderance of flow in one
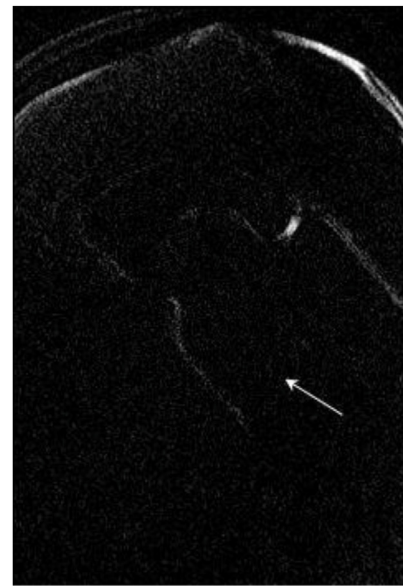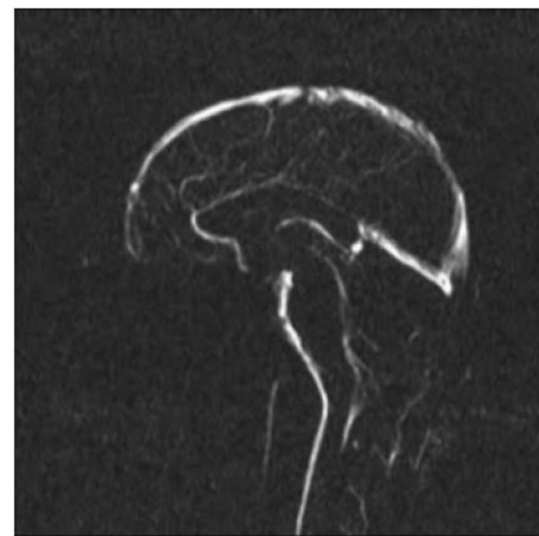
Fig. 4. Selected image from an MRI of the brain including velocity encoded phase contrast flow study sequence (a). This reveals tonsillar descent of 17 mm. The absence of CSF flow posterior to the cervico-medullary junction is marked by the arrow (a). A normal appearing CSF flow sequence of comparison (b) (Battal et al., 2011).

direction, and synchronous bidirectional flow (Quigley et al., 2004). Abnormal pulsatile motion of the cerebellar tonsils are observed in symptomatic CM-I patients, and the amplitude of tonsillar pulsation and the degree of arachnoid space reduction improves following surgery. (Wolpert et al., 1994; Pujol et al., 1995).

CSF dynamic studies have been used to distinguish symptomatic from asymptomatic CM-I patients, yet the evidence remains inconsistent (Hofkes et al., 2007; Krueger et al., 2010). However, CSF velocity patterns in CM-I patients may be useful in predicting surgical improvement (Bhadelia et al., 1995; McGirt et al., 2006; Ventureyra et al., 2003; Armonda et al., 1994). A group of patients with normal preoperative hindbrain CSF flow were 4.8-fold more likely to experience symptom recurrence post-operatively, irrespective of their degree of tonsillar herniation or presence of syringomyelia, whilst complete CSF flow obstruction before surgery was associated with the long-term resolution of symptoms (McGirt et al., 2006). At present, dynamic studies provide an assessment of the degree of obstruction at the craniocervical junction,

and may help predict surgical suitability. They are not useful in every case, but obstructed flow can be used to help predict a more successful surgical outcome in borderline cases, or for follow up assessment in symptom recurrence (Fig. 4).

2.9. Dynamic mobility studies

CM-I has been linked to hypermobility syndromes, such as Ehlers-Danlos, and Marfans syndrome. (Henderson et al., 2017; Milhorat et al., 2010a). Hypermobility syndromes are a heterogenous group of inherited connective tissue disorders characterized by joint hypermobility, skin extensibility, and tissue fragility (Forghani, 2019). It has been suggested that hypermobility or instability at the craniocervical junction causes basiler invagination, or stretching of the brainstem producing symptoms[54-56]. Assessments have included using flexion and extension in an upright MRI, although the measurements can be made on a standard supine c-spine flexion MRI to include the Clivo-axial angle (CXA), the Harris, and the Grabb Oakes (pBC2) measurements (Henderson FC et al., 2018; Henderson et al., 2019; Henderson et al., 2020) (Fig. 5). These

measurements, the assessment of instability rather than hypermobility, and the optimal treatment remain controversial (Brodbelt and Flint, 2017).

Instability has been suggested to be the cause of the symptoms in CM-I (Goel, 2015a). The initial study was based on a group of patients with a very high level of basiler invagination and craniocervical abnormalitites in a centre taking referrals, often after initial CM-I decompressive surgery, from a large population base (Goel, 2015b). Other authors have not found this to be representative of the CM-I population at large. These studies and those related to patients with hypermobility, do suggest that hypermobility or instability at the craniocervical junction may be present in some patients and should be evaluated both clinically and radiologically.

There has been interest in the use of upright MRI in CM-I, as some patients are only symptomatic when erect, and dynamic views can be easier to acquire (Botchu et al., 2018). The tonsils may be lower when upright, and in severely orthostatic symptomatic patients, this may help evaluate surgical options.
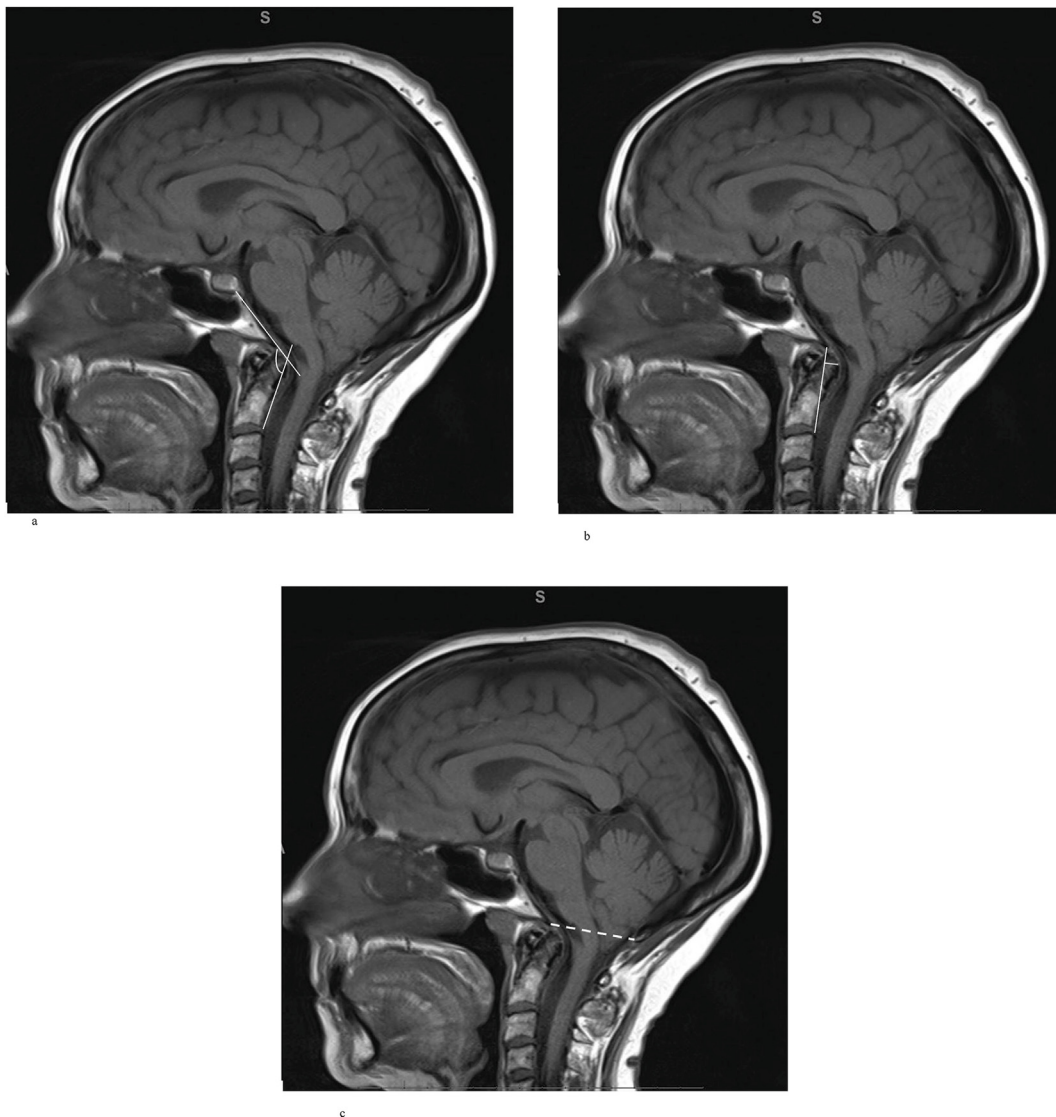

Fig. 5. (a) The Clivoaxial angle (CXA) measures flexion at the craniocervical junction by measuring the angle between a line drawn along the clivus with that along the posterior margin of the odontoid peg and is said to be abnormal if on a flexion C-spine MRI it is < 135°. (b) The pBC2 line examines the dorsal protrusion of the odontoid peg, and is said to be abnormal if ≥ 9 mm. (c) McRae's line is the line drawn across the inferior margin of the foramen magnum, and is used to measure tonsilar descent.

2.10. Magnetic resonance imaging (MRI) – spinal evaluation

2.10.1. Syringomyelia

Up to 50% of patients with a symptomatic CM-I will develop a syrinx (Holly and Batzdorf, 2019) (Fig. 3). Syrinxes are best shown on sagittal MR T2-weighted imaging of the whole spinal cord, accompanied by axial T2 views. Contrast-enhancing sequences in patients with a syrinx in the absence of a CM-I are mandatory to look for an associated tumour, but are less useful when a CM-I is present (Timpone and Patel, 2015). Syrinx formation is more common in patients with greater tonsillar herniation, and CSF flow obstruction, and are most common at the C4 to C6 levels (Strahle et al., 2011; Strahle et al., 2015). A terminal syrinx, located in the distal spinal cord, is often associated with a tethered cord, or spinal dysraphism. Preoperative radiological identification of a syrinx, even in the absence of associated symptoms, aids surgical decision making and post operative assessment of success.

2.10.2. Tethered cord syndrome

Tethered cord syndrome (TCS) occurs in 14% of patients with CM-I (Milhorat et al., 2009). Whilst the term tethered cord can indicate a fixed area of spinal cord, TCS refers to tethering of the spinal cord at the lumber level (Hertzler et al., 2010). This is usually diagnosed when the conus medullaris is caudal to L2, but other radiological signs used include a thickened or fatty filum, spina bifida oculta, terminal syringomyelia, a lower thoracic scoliosis, and a dorsal position of the filum on prone or upright MRI (McGirt et al., 2006). Lumbar MRI demonstrates the level of the conus medullaris, the thickness of the filum terminale, and any associated dysraphic elements. Further assessment with CT for more complex bony abnormalities, and electrophysiology for urological impairment, is sometimes required. Whilst release of a 'classical' radiologically tethered cord in a patient with a symptomatic CM-I and/or terminal syrinx is accepted treatment, some authors will divide a normal filum in treating patients with CM-I, but this remains controversial (Seki et al., 2016; Tandon et al., 2014).

3. Conclusions

The majority of CM-I diagnoses are incidental findings but can lead to great anxiety on the part of the non specialist physician and patient. A MRI brain and cervical spine is indicated in all such radiologically labelled CM-1. The radiology report should attempt to comment on any underlying cause for CM-1, the degree of tonsillar descent, impaction and obliteration of CSF spaces. All such cases should be discussed with the appropriate specialist and clinically assessed as appropriate by a detailed history and examination. In radiologically significant CM-I cases and/or symptomatic patients, MRI brain and entire spine is indicated. Radiological significance is denoted by the presence of significant tonsillar impaction in CM-I resulting in tonsillar asymmetry or loss of CSF spaces around the tonsillar region, or other associated structural abnormalities. Dynamic views of fluid flow, and flexion/extension MRI and localised detailed CT scanning can also aid in surgical decision making and help predict surgical success. Development of a grading scheme based on specific MRI characteristics may help identify patients likely to develop symptoms and predict surgical outcomes.

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Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval

This article does not contain any studies with human participants performed by any of the authors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Aboulezz, A.O., Sartor, K., Geyer, C.A., Gado, M.H., 1985. Position of cerebellar tonsils in the normal population and in patients with chiari malformation: a quantitative approach with MR imaging. J. Comput. Assist. Tomogr. 9 (6), 1033–1036.

Armonda, R.A., Citrin, C.M., Foley, K.T., Ellenbogen, R.G., 1994. Quantitative cine-mode magnetic resonance imaging of chiari i malformations: an analysis of cerebrospinal fluid dynamics. Neurosurgery 35 (2), 214–224.

Badie, B., Mendoza, D., Batzdorf, U., 1995. Posterior fossa volume and response to suboccipital decompression in patients with chiari i malformation. Neurosurgery 37 (2), 214–218.

Battal, B., Kocaoglu, M., Bulakbasi, N., Husmen, G., Tuba Sanal, H., Tayfun, C., 2011. Cerebrospinal fluid flow imaging by using phase-contrast MR technique [Internet]. In: British Journal of Radiology. Br J Radiol, vol. 84 [cited 2021 May 21]. pp. 758–65. Available from: https://pubmed.ncbi.nlm.nih.gov/21586507/.

Bhadelia, R.A., Bogdan, A.R., Wolpert, S.M., Lev, S., Appignani, B.A., Heilman, C.B., 1995. Cerebrospinal fluid flow waveforms: analysis in patients with Chiari I malformation by means of gated phase-contrast MR imaging velocity measurements. Radiology 196 (1), 195–202.

Botchu, R., Bharath, A., Davies, A.M., Butt, S., James, S.L., 2018. Current concept in upright spinal MRI [Internet]. In: European Spine Journal, vol. 27. Springer Verlag [cited 2021 Feb 16]. pp. 987–93. Available from: https://pubmed.ncbi.nlm.nih.gov/28936611/.

Brockmeyer, D.L., 2011. The complex Chiari: issues and management strategies [Internet] Neurol. Sci. [cited 2021 Feb 13];32(SUPPL. 3). Available from: https://pubmed.ncbi.nlm.nih.gov/21822705/.

Brodbelt, A.R., Flint, G., 2017. Ehlers Danlos, complex Chiari and cranio-cervical fixation: how best should we treat patients with hypermobility? [Internet]. In: British Journal of Neurosurgery, vol. 31. Taylor and Francis Ltd [cited 2021 Feb 16]. pp. 397–8. Available from: https://pubmed.ncbi.nlm.nih.gov/28961036/.

Cahan, L.D., Bentson, J.R., 1982. Considerations in the diagnosis and treatment of syringomyelia and the Chiari malformation [Internet] J. Neurosurg. [cited 2020 Sep 21];57(1):24–31. Available from: https://pubmed.ncbi.nlm.nih.gov/7086497/.

Chazen, J.L., Talbott, J.F., Lantos, J.E., Dillon, W.P., 2014 Oct 1. MR myelography for identification of spinal CSF leak in spontaneous intracranial hypotension [Internet] Am. J. Neuroradiol. [cited 2021 Feb 14];35(10):2007–12. Available from: https://pubmed.ncbi.nlm.nih.gov/24852289/.

Chiari, H., 1895. Ueber verinderungen des kleinhirns, des pons und der medulla oblongata in folge yon congenitaler hydrocephalie des grosshirns. Denschr Akad Wiss Wien 63, 71–116.

Decq, P., Guérinel, C.L., Sol, J.C., Brugières, P., Djindjian, M., Nguyen, J.P., 2001 Nov. Chiari I malformation: a rare cause of noncommunicating hydrocephalus treated by third ventriculostomy [Internet] J. Neurosurg. [cited 2020 Apr 11];95(5):783–90. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11702868.

Dufton, J., Habeeb, S., Heran, M., Mikulis, D., Islam, O., 2011 May 1. Posterior fossa measurements in patients with and without chiari i malformation. Can. J. Neurol. Sci. 38 (3), 452–455.

Dyste, G.N., Menezes, A.H., VanGilder, J.C., 1989 Aug 1. Symptomatic Chiari malformations. An analysis of presentation, management, and long-term outcome [Internet] J. Neurosurg. [cited 2020 Sep 20];71(2):159–68. Available from: https://thejns.org/view/journals/j-neurosurg/71/2/article-p159.xml.

Elster, A.D., Chen, M.Y.M., 1992. Chiari I malformations: clinical and radiologic reappraisal. Radiology 183 (2), 347–353.

Forghani, I., 2019. Updates in clinical and genetics aspects of hypermobile ehlers danlos syndrome [Internet]. In: Balkan Medical Journal, vol. 36. Galenos Publishing House [cited 2020 Sep 21]. pp. 12–6. Available from:/pmc/articles/PMC6335943/?report=abstract.

Goel, A., 2015 Feb 1. Is atlantoaxial instability the cause of Chiari malformation? Outcome analysis of 65 patients treated by atlantoaxial fixation [Internet] J. Neurosurg. Spine [cited 2021 Feb 16];22(2):116–27. Available from: https://pubm ed.ncbi.nlm.nih.gov/25415487/.

Goel, A., 2015b. Cranioverbral junction instability: a review of facts about facets [Internet]. In: Asian Spine Journal, vol. 9. Korean Society of Spine Surgery [cited 2021 Apr 15]. pp. 636–44. Available from: https://www.ncbi.nlm.nih.gov/pmc/artic les/PMC4522459/.

Grant, R., M Hadley, D., MacPherson, P., Condon, B., Patterson, J., Bone, I., et al., 1987 Aug 1. Syringomyelia: cyst measurement by magnetic resonance imaging and comparison with symptoms, signs and disability [Internet] J. Neurol. Neurosurg. Psychiatry [cited 2020 Sep 21];50(8):1008–14. Available from: http://jnnp .bmj.com/.

Hadley, D.M., 2002. The Chiari malformations. In: Neurology in Practice, vol. 72. BMJ Publishing Group Ltd, pp. ii38–40.

Haughton, V.M., Korosec, F.R., Medow, J.E., Dolar, M.T., Iskandar, B.J., 2003 Feb. Peak systolic and diastolic CSF velocity in the foramen magnum in adult patients with Chiari I malformations and in normal control participants [Internet] AJNR Am J Neuroradiol [cited 2019 Dec 7];24(2):169–76. Available from: http://www.ncbi.nlm. nih.gov/pubmed/12591629.

Hayhurst, C., Osman-Farah, J., Das, K., Mallucci, C., 2008. Initial management of hydrocephalus associated with Chiari malformation Type I-syringomyelia complex via endoscopic third ventriculostomy: an outcome analysis [Internet]. In: Journal of Neurosurgery. J Neurosurg, vol. 108 [cited 2021 Feb 16]. pp. 1211–4. Available from: https://pubmed.ncbi.nlm.nih.gov/18518729/.

Hayward, R., 2003 Jun 7. VOMIT (victims of modern imaging technology)"an acronym for our times. BMJ 326 (7401), 1273.

Henderson, F.C., Austin, C., Benzel, E., Bolognese, P., Ellenbogen, R., Francomano, C.A., et al., 2017 Mar 1. Neurological and spinal manifestations of the Ehlers-Danlos syndromes [Internet] Am. J. Med. Genet. Part C Semin Med Genet. https://doi.org/ 10.1002/ajmg.c.31549 [cited 2020 Jun 6];175(1):195–211. Available from:

Henderson, F.C., Francomano, C.A., Koby, M., Tuchman, K., Adcock, J., Patel, S., 2019 Dec 1. Cervical medullary syndrome secondary to craniocervical instability and ventral brainstem compression in hereditary hypermobility connective tissue disorders: 5-year follow-up after craniocervical reduction, fusion, and stabilization [Internet] Neurosurg. Rev. [cited 2020 Sep 21];42(4):915–36. Available from::, /pmc/articles/PMC6821667/?report=abstract.

Henderson, F., Rosenbaum, R., Narayanan, M., Mackall, J., Koby, M., 2020. Optimizing alignment parameters during craniocervical stabilization and fusion: a technical note [Internet] Cureus. Mar 2 [cited 2020 Sep 21];12(3). Available from:, /pmc/articles/ PMC7112711/?report=abstract.

Henderson Fc, Sr, Henderson Jr., F.C., Wilson, W.A., et al., IV, 2018. Utility of the clivo-axial angle in assessing brainstem deformity: pilot study and literature review [Internet] Neurosurg. Rev. [cited 2020 Sep 21];41(1):149. Available from:

Hertzler, D.A., DePowell, J.J., Stevenson, C.B., Mangano, F.T., 2010 Jul. Tethered cord syndrome: a review of the literature from embryology to adult presentation [Internet] Neurosurg. Focus [cited 2020 Apr 11];29(1):1–9. Available from: http://www.ncbi. nlm.nih.gov/pubmed/20593997.

Hofkes, S.K., Iskandar, B.J., Turski, P.A., Gentry, L.R., McCue, J.B., Haughton, V.M., 2007 Nov. Differentiation between symptomatic Chiari I malformation and asymptomatic tonsillar ectopia by using cerebrospinal fluid flow imaging: initial estimate of imaging accuracy. Radiology 245 (2), 532–540.

Holly, L.T., Batzdorf, U., 2019. Chiari malformation and syringomyelia [Internet]. In: Journal of Neurosurgery: Spine, vol. 31. American Association of Neurological Surgeons [cited 2020 Apr 6]. pp. 619–28. Available from: http://www.ncbi.nlm. gov/pubmed/31675698.

Honan, W.P., Williams, B., 1993. Sensory loss in syringomyelia: not necessarily dissociated [Internet] J. R. Soc. Med. [cited 2020 Sep 21];86(9):519–20. Available from: /pmc/articles/PMC1294098/?report=abstract.

Hwang, S.W., Samdani, A.F., Jea, A., Raval, A., Gaughan, J.P., Betz, R.R., et al., 2012 Aug 18. Outcomes of Chiari I-associated scoliosis after intervention: a meta-analysis of the pediatric literature [Internet Child's Nerv. Syst. [cited 2021 Feb 14];28(8):1213–9. Available from: https://link.springer.com/article/10.1007/s00381-012-1739-3.

Jussila, M.-P., Nissilä, J., Vakkuri, M., Olsén, P., Niinimäki, J., Leinonen, V., et al., 2021. Preoperative measurements on MRI in Chiari 1 patients fail to predict outcome after decompressive surgery. Acta Neurochir. 1637 [Internet]. 2021 May 11 [cited 2021 Oct 26];163(7):2005–14. Available from: https://link.springer.com/article/10.1007 /s00701-021-04842-y.

Karagöz, F., Izgi, N., Sencer, S.K.I.I., 2002. Morphometric measurements of the cranium in patients with Chiari type I malformation and comparison with the normal population. Acta Neurochir. 144 (2), 165–171.

Krueger, K.D., Haughton, V.M., Hetzel, S., 2010 Nov. Peak CSF velocities in patients with symptomatic and asymptomatic Chiari I malformation. Am. J. Neuroradiol. 31 (10), 1837–1841.

Langridge, B., Phillips, E., Choi, D., 2017 [Internet]. Chiari Malformation Type 1: A Systematic Review of Natural History and Conservative Management, vol. 104. World Neurosurgery. Elsevier Inc. [cited 2020 Apr 11]. pp. 213–9. Available from: http ://www.ncbi.nlm.nih.gov/pubmed/28435116

Li, H.Y., Wang, P.C., Hsu, C.Y., Chen, N.H., Fang, T.J., 2005 Apr. Changes of sleep-disordered breathing after laryngeal surgery in patients with bilateral vocal fold paralysis. Eur. Arch. Oto-Rhino-Laryngol. 262 (4), 294–297.

Malfait, F., Francomano, C., Byers, P., Belmont, J., Berglund, B., Black, J., et al., 2017. The 2017 International Classification of the Ehlers–Danlos Syndromes [Internet]. Am J Med Genet Part A Semin Med Genet. Mar 1 [cited 2021 Feb 16];175(1):8–26. Available from: https://pubmed.ncbi.nlm.nih.gov/28306229/.

Mariwalla, N.R., Boydston, W.R., Chern, J.J., 2014. Newer subsets: chiari 0 and chiari 1.5 malformations. In: The Chiari Malformations. Springer, New York, pp. 241–246.

McGirt, M.J., Nimjee, S.M., Fuchs, H.E., George, T.M., 2006 Jul. Relationship of cine phase-contrast magnetic resonance imaging with outcome after decompression for Chiari I malformations. Neurosurgery 59 (1), 140–145.

Mea, E., Chiapparini, L., Leone, M., Franzini, A., Messina, G., Bussone, G., 2011 Aug 6. Chronic daily headache in the adults: differential diagnosis between symptomatic Chiari I malformation and spontaneous intracranial hypotension [Internet] Neurol. Sci. [cited 2020 Sep 16];32(SUPPL. 3):291–4. Available from: https://link.springe r.com/article/10.1007/s10072-011-0698-x.

Meadows, J., Kraut, M., Guarnieri, M., Haroun, R.I., Carson, B.S., 2000. Asymptomatic Chiari Type I malformations identified on magnetic resonance imaging. J. Neurosurg. 92 (6), 920–926.

Mikulis, D.J., Diaz, O., Egglin, T.K., Sanchez, R., 1992. Variance of the position of the cerebellar tonsils with age: preliminary report. Radiology 183 (3), 725–728.

Milhorat, T.H., Chou, M.W., Trinidad, E.M., Kula, R.W., Mandell, M., Wolpert, C., et al., 1999 May. Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. Neurosurgery 44 (5), 1005–1017.

Milhorat, T.H., Bolognese, P.A., Nishikawa, M., Francomano, C.A., McDonnell, N.B., Roonprapunt, C., et al., 2009 Jul. Association of Chiari malformation type I and tethered cord syndrome: preliminary results of sectioning filum terminale. Surg. Neurol. 72 (1), 20–35.

Milhorat, T.H., Nishikawa, M., Kula, R.W., Dlugacz, Y.D., 2010 Jul. Mechanisms of cerebellar tonsil herniation in patients with Chiari malformations as guide to clinical management [Internet] Acta Neurochir. [cited 2021 Feb 14];152(7):1117–27. Available from: /pmc/articles/PMC2887504/.

Milhorat, T.H., Nishikawa, M., Kula, R.W., Dlugacz, Y.D., 2010 Jul. Mechanisms of cerebellar tonsil herniation in patients with Chiari malformations as guide to clinical management. Acta Neurochir. 152 (7), 1117–1127.

Nishikawa, M., Sakamoto, H., Hakuba, A., Nakanishi, N., Inoue, Y., 1997. Pathogenesis of Chiari malformation: a morphometric study of the posterior cranial fossa. J. Neurosurg. 86 (1), 40–47.

Noudel, R., Gomis, P., Sotoares, G., Bazin, A., Pierot, L., Pruvo, J.P., et al., 2011 Sep. Posterior fossa volume increase after surgery for Chiari malformation Type I: a quantitative assessment using magnetic resonance imaging and correlations with the treatment response - clinical article. J. Neurosurg. 115 (3), 647–658.

Oestreich, A.E., Young, L.W., Poussaint, T.Y., 1998 [Internet]. Scoliosis Circa 2000: Radiologic Imaging Perspective. I. Diagnosis and Pretreatment Evaluation, vol. 27. Skeletal Radiology. Skeletal Radiol [cited 2021 May 20]. pp. 591–605. Available from: https://pubmed.ncbi.nlm.nih.gov/9867177/.

Ohara, S., Nagai, H., Matsumoto, T., Banno, T., 1988. MR imaging of CSF pulsatory flow and its relation to intracranial pressure. J. Neurosurg. 69 (5), 675–682.

Orakdogen, M., Emon, S.T., Erdogan, B., Somay, H., 2015. Fourth ventriculostomy in occlusion of the foramen of Magendie associated with chiari malformation and syringomyelia. NMC Case Rep J 2 (2), 72.

Pujol, J., Roig, C., Capdevila, A., Pou, A., Martí-Vilalta, J.L., Kulisevsky, J., et al., 1995 Sep. Motion of the cerebellar tonsils in Chiari type I malformation studied by cine phase-contrast MRI [Internet] Neurology [cited 2019 Dec 7];45(9):1746–53. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7675239.

Quigley, M.F., Iskandar, B., Quigley, M.E., Nicosia, M., Haughton, V., 2004 Jul. Cerebrospinal fluid flow in foramen magnum: temporal and spatial patterns at MR imaging in volunteers and in patients with Chiari I malformation. Radiology 232 (1), 229–236.

Seki, T., Hida, K., Yano, S., Sasamori, T., Hamauch, S., Koyanagi, I., et al., 2016. Surgical outcome of children and adolescents with tethered cord syndrome. Asian Spine J 10 (5), 940–944.

Sekula, R.F., Jannetta, P.J., Casey, K.F., Marchan, E.M., Sekula, L.K., McCrady, C.S., 2005 Dec 18. Dimensions of the posterior fossa in patients symptomatic for Chiari I malformation but without cerebellar tonsillar descent. Cerebrospinal Fluid Res. 2.

Smith, B.W., Strahle, J., Bapuraj, J.R., Muraszko, K.M., Garton, H.J.L., Maher, C.O., 2013 Sep. Distribution of cerebellar tonsil position: implications for understanding Chiari malformation. J. Neurosurg. 119 (3), 812–819.

Spinos, E., Laster, D.W., Moody, D.M., Ball, M.R., Witcofski, R.L., Kelly, D.L., 1985. MR evaluation of Chiari I malformations at 0.15 T. Am. J. Roentgenol. 144 (6), 1143–1148.

Stovner, L.J., Bergan, U., Nilsen, G., Sjaastad, O., 1993 Jan. Posterior cranial fossa dimensions in the Chiari I malformation: relation to pathogenesis and clinical presentation. Neuroradiology 35 (2), 113–118.

Strahle, J., Muraszko, K.M., Kapurch, J., Bapuraj, J.R., Garton, H.J.L., Maher, C.O., 2011 Aug. Chiari malformation Type I and syrinx in children undergoing magnetic resonance imaging: clinical article. J. Neurosurg. Pediatr. 8 (2), 205–213.

Strahle, J., Muraszko, K.M., Garton, H.J.L., Smith, B.W., Starr, J., Kapurch, J.R., et al., 2015 Jul 1. Syrinx location and size according to etiology: identification of Chiari-associated syrinx [Internet] J. Neurosurg. Pediatr. [cited 2020 Apr 6];16(1):21–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25837888.

Tandon, V., Garg, K., Kumar, R., Mahapatra, A., Sharma, B., 2014. Management of adult tethered cord syndrome: our experience and review of literature [Internet] Neurol. India [cited 2020 Jun 6];62(2):137. Available from: http://www.neurology india.com/text.asp?2014/62/2/137/132329.

Taylor, F.R., Larkins, M.V., 2002. Headache and Chiari I malformation: clinical presentation, diagnosis, and controversies in management [Internet]. In: Current Pain and Headache Reports, vol. 6. Springer [cited 2021 Apr 19]. pp. 331–7. Available from: https://link.springer.com/article/10.1007/s11916-002-0056-z.

Timpone, V.M., Patel, S.H., 2015 May 1. MRI of a syrinx: is contrast material always necessary? [Internet] Am. J. Roentgenol. cited 2020 May 31];204(5):1082–5. Available from: http://www.ajronline.org/doi/10.2214/AJR.14.13310.

Tubbs, R.S., McGirt, M.J., Oakes, W.J., 2003 Aug 1. Surgical experience in 130 pediatric patients with Chiari I malformations [Internet] J. Neurosurg. [cited 2020 Apr 6]; 99(2):291–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12924703.

Urbizu, A., Poca, M.A., Vidal, X., Rovira, A., Sahuquillo, J., Macaya, A., 2014. MRI-based morphometric analysis of posterior cranial fossa in the diagnosis of chiari malformation type I. J. Neuroimaging 24 (3), 250–256.

Ventureyra, E.C.G., Aziz, H.A., Vassilyadi, M., 2003 Feb 1. The role of cine flow MRI in children with Chiari I malformation. Child's Nerv. Syst. 19 (2), 109–113.

Whedon, J.M., Glassey, D., 2009. Cerebrospinal fluid stasis and its clinical significance. Alternative Ther. Health Med. 15, 54–60.

Wilson, M.H., 2016. Monro-Kellie 2.0: the dynamic vascular and venous pathophysiological components of intracranial pressure. In: Journal of Cerebral Blood Flow and Metabolism, vol. 36. Nature Publishing Group, pp. 1338–1350.

Wolpert, S.M., Bhadelia, R.A., Bogdan, A.R., Cohen, A.R., 1994. Chiari I malformations: assessment with phase-contrast velocity MR. Am. J. Neuroradiol. 15 (7), 1299–1308.