Chiari Malformation Type 1: A Systematic Review of Natural History and Conservative Management

Abstract

OBJECTIVE:

To determine the natural history of unoperated Chiari type 1 malformation (CM-1) in adults.

METHODS:

A literature search was performed following PRISMA guidelines using the electronic databases PubMed, SCOPUS, the Cochrane foundation and Web of Science. No time limits were set during the search. The key words "Chiari Malformation 1", "Conservative", "Non-operative", "Natural History", "Non-surgical" and "Asymptomatic" were used. Articles were excluded if they related solely to pediatric cases (<18 years of age) or patients with additional congenital syndromes. Non-English-language articles, commentaries, textbooks or opinion articles were also excluded.

RESULTS:

Ataxia and headaches tend to improve after surgery, but little is known about the natural history of symptoms in patients who do not undergo surgery, and in asymptomatic individuals.

In symptomatic patients who did not undergo surgery, headaches and nausea often improved, whereas ataxia and sensory disturbance tended not to improve spontaneously. There are scattered case reports of acute respiratory failure, but insufficient evidence to promote surgery to avoid the potential for sudden deterioration in asymptomatic individuals.

Most asymptomatic individuals with CM-1 remain asymptomatic (93.3%), even in the presence of syringomyelia.

CONCLUSIONS:

The natural history of mild symptomatic and asymptomatic CM-1 in adults is relatively benign and non-progressive, therefore the decision to perform surgical decompression should be based

on the severity and duration of a patient's symptoms at presentation. It is reasonable to observe a patient with mild or asymptomatic symptoms, even in the presence of significant tonsillar descent or syringomyelia.

<u>Introduction</u>

The Arnold-Chiari malformation type 1, which we will refer to as Chiari malformation 1 (CM-1), was originally defined by Hans Chiari as an "elongation of the tonsils and the medial parts of the inferior lobes of the cerebellum into cone-shaped projections which accompany the medulla oblongata into the spinal canal".[1] A common treatment for symptomatic CM-1 is foramen magnum decompression, and although there is debate around the technical aspects of surgery, the outcomes and risks of surgery are well documented. However, little is known about the natural history of CM-1 without surgery in symptomatic and asymptomatic individuals, and appreciation of this information is necessary to decide the merits of surgical management. CM-1 is uncommon in adults, and there is little clear evidence to guide management; we present the first systematic review of the natural history and conservative management of CM-1 in adults, to help surgeons and patients decide when to perform surgery for CM-1.

Objectives

We reviewed published studies of CM-1 to determine the following:

    a) The presenting features of CM-1 in adults

    b) Commonly used indications for surgical intervention

    c) The natural history of CM-1 in adults

    d) The natural history of asymptomatic incidental CM-1

    e) The natural history syringomyelia with CM-1

Methods:

Data sources and search strategy

We performed a systematic literature review in the format recommended by the Preferred Reporting Items for Systematic Reviews and Meta-analyses Guidelines.[2]

A literature search was performed using the electronic databases PubMed, SCOPUS, The Cochrane foundation and Web of Science, no time limits were set during the search. Indexes were accessed between 2/2/16 and 22/2/16.

A search strategy was created using the terms detailed in **Table 1**. Results were reviewed to exclude duplicates, those not published in the English language, and those that were irrelevant in topic (**Fig. 1**). The full texts of the remaining articles were then reviewed in detail and outlined in this systematic review, with the reference lists of these full articles being hand-searched for any additional articles which were missed by the original search strategies.

Study selection and analysis

We included any article related to CM-1 but excluded those relating solely to pediatric cases (<18 years of age), or patients with additional congenital syndromes. Articles that included both pediatric and adult populations were retained and the relevant adult data was included. Articles were analyzed with a predetermined, standardized appraisal pro forma.

Results:

Selected Articles

Our search strategy (**Table 1**) identified 344 articles which were reduced to 198 after excluding duplicates. After title and abstract review, the number of relevant articles was reduced to 44. Following full-text review a further 33 articles were excluded, leaving 11 articles for detailed inclusion in this systematic review.[3-13] Four further articles were identified from article bibliographies,[14-17] therefore a total of 15 articles were identified for inclusion in this systematic review (**Fig. 1**). **Table 2** shows the breakdown of reasons for article exclusion and **Table 3** outlines the characteristics of the reviewed papers. Some heterogeneity exists in the definition of CM-1 used in published articles, **Table 4** provides a summary of the definitions used in the reviewed papers.

Presenting features of Chiari Malformation 1 in Adults

CM-1 presents in numerous ways. Headaches, of either the cough or migrainous type, and paraesthesia are the most common presenting symptoms. Other common presenting symptoms include nausea, dysphagia, apnoea, clonus, cerebellar symptoms, drop attacks, muscle atrophy and dysphonia (**Table 5**). Case reports exist of more unusual presentations such as orthopnoea[18], vertigo[19] and diplopia[20]. Additionally, a number of patients are found incidentally on MRI scans.[21]

The literature search found 21 papers with details on the presenting symptoms of one or more cases of CM-1.[4-6,8-10,15,16,19-30] Of these, 13 discussed fewer than 10 patients,[6,8,10,15,16,18-20,22,25-28] with the majority of these being case reports. Four looked at between 10 and 40 patients[3,9,24,29] and three looked at over 40 patients.[4,5,23] One paper reviewed patients with syringomyelia, most of whom had CM-1 but not exclusively so. However, because the data did not differentiate between the presenting symptoms of those with Chiari 1 malformations and those without we were unable to include the details in our review.[31]

Killeen et al. reported 47 adult patients who were not recommended for surgery. The 21 pediatric patients were not included. Nine (19.2%) presented with cough headache only, 14 (29.8%) presented with migrainous headache only and 18 (38.3%) presented with both cough and

migrainous headache. Paraesthesia was the most common presenting symptom with 27 patients (57.5%), closely followed by ataxia which was seen in 26 patients (55.3%).[5] As these patients were not recommended for surgery this dataset is likely to include patients with less severe symptoms than a more typical group of patients including those that had surgery.

Chavez et al. identified 68 conservatively treated and 109 surgically treated patients. Twenty-nine percent of the patients were under 18 years of age. It was not possible to separate out the pediatric from the adult patients in their data. For patients managed conservatively 11 (21%) presented with cough headaches, 20 (40%) with migraine headaches and 19 (38%) with both type of headache. 31 (45.6%) had paraesthesia and 28 (41.8%) had cerebellar symptoms or signs.[4] Despite including a significant number of pediatric patients these numbers are broadly similar to those described by Killeen et al. For those that had surgical treatment, 56 (68.3%) had a cough headache only, 14 (17.1%) had a migraine headache only and 12 (14.6%) had both types of headache. Paraesthesia was seen in 35 (32.1%) and cerebellar symptoms or signs were seen in 8 (7.3%).[5]

Hayhurst et al looked at 96 patients with Chiari malformations. 83 had Chiari 1 malformations and 13 had Chiari 2 malformations. It was not possible to identify which patients had Chiari 1 malformations and which had Chiari 2 malformations from this paper. 63 (67%) of patients presented with headache, 13 (13.5%) of which presented with cough induced headaches only. Hayhurst et al did not separate the number of patients with migraine type headaches or both migraine and cough headaches, making comparison with the other papers difficult. Paraesthesia was seen in 34 (35.4%) of patients and unsteadiness or ataxia was seen in 13 (13.5%).[23]

There were also case reports of patients presenting with rare symptoms. While sleep apnoea is seen in a small proportion of patients, Mangubat et al. recorded a case of orthopnoea due to CM-1.[18] Klein et al. reported a case of vertigo and vestibular difficulties[19] and Furuya et al reported six cases of vertigo.[29] Patients can also present with visual problems. Bindal et al. looked at 27 patients and found that seven had nystagmus,[3] and Zainon et al. reported one patient who had diplopia, vocal cord prolapse and giddiness.[20] Decq et al. reported two cases where visual problems were presenting features. One patient had diplopia and on examination had

papilledema. A second patient had a 1 hour episode of blindness which resolved spontaneously.[28]

Common indications for surgical intervention

Many papers were identified in the systematic review which specified presenting symptoms of CM-1, but it was difficult to ascertain the exact symptom(s) that precipitated the decision to operate. However, five papers did discuss indications for surgery in various formats. Three papers mentioned the indications that were used in their study or discussed the indications they consider generally accepted.[5,12,4] Three papers assessed the usefulness of various factors in indicating surgery (Ucar et al, Bindal et al and Chavez et al)[3,4,31]. **Table 6** provides a summary of the criteria used for surgical intervention.

There was no consensus on the exact indications for surgery in CM-1. Common indications include:

"(1) cough associated headaches that impact quality of life, (2) large or enlarging syrinx, and (3) objective abnormal neurological findings or myelopathy. CSF flow abnormalities, tonsillar descent, or cervicomedullary crowding serve as adjunct criteria."[4]

Ramón et al. stated that in asymptomatic patients it is widely agreed that surgery is not necessary but in patients with progressive posterior fossa or spinal cord signs, hydrocephalus or syringomyelia surgery is recommended.[12] However, there are several case reports which identified patients with syringomyelia who did not undergo surgery.[6] Indeed, it is known that syringomyelia can be found with a significant prevalence in the general population and these rarely require surgery.[15] Ramón et al. also state that in patients only presenting with cough headaches they have found that surgery was performed in 25% of cases.[6] This demonstrates a degree of variability in the indications for surgery.

This uncertainty has led to several studies to try and identify the best indications for surgery and to produce evidence based guidelines on when it is best to operate. Chavez et al. compared symptom improvement in patients who either did or did not have surgery in a retrospective uncontrolled series. Headaches seemed to suggest the greatest benefit, with 95% of patients with

cough headache improving after surgery but only 40% improving with conservative treatment (p<0.05). Ninety-three percent of other headaches improved with surgery and 61.5% with conservative treatment (p=0.09).[4] This is supported by Killeen et al. who found that the presence of cough headaches was a potentially negative indicator for improvement.[5]

Symptoms of ataxia improved in 21% of conservatively treated patients but 87.5% of surgically treated patients (p<0.05). This would seem to suggest that ataxia is a strong indication for surgery. However, of the 36 patients in the study with ataxia, only eight were operated on suggesting that ataxia is not commonly felt to be a strong indication for surgery. Paraesthesia was the only other symptom to find a difference in improvement between the surgical and conservative groups. Seventy-seven percent of patients improved after surgery whereas only 42% improved with conservative management.[5] However, this was not a randomized study and the selection bias may lead to difficulty in applying these findings, and whether these symptoms were independently associated with improvement after surgery.

Bindal et al. produced a classification system to predict outcomes and help determine the appropriate surgical management. Using 21 cases they found that after surgery symptoms from brainstem compression were significantly improved whereas symptoms from syringomyelia stabilised or only slightly improved. They therefore suggested that symptoms of brainstem compression should be a stronger indication for surgery compared to symptoms of syringomyelia.[3]

Ucar et al. suggested using a novel imaging technique called "Sampling Perfection with Application optimized Contrast using different flip angle Evolutions" (SPACE) to image tonsillar motion and use this information to determine suitability for surgery.[31]

Natural History of Unoperated Symptomatic Chiari Malformation 1
The natural history of symptomatic CM-1 in adults is poorly documented, with most studies investigating pediatric cases or outcomes after surgery. Our literature review identified seven papers[4-9, 16] of relevance to this question but most available evidence originates from two publications – Killeen et al. and Chavez et al.[4, 5] These papers suggested that many patients

selected for conservative management as a result of mild symptoms will either improve or not deteriorate after long term follow up, with serious events being infrequent.

Killeen et al found that the majority (63.8%) of adult patients who were selected for conservative management on the basis of mild symptoms either improved or remained unchanged over time (average follow-up of 4.9 ± 2.9 years), with 25.5% reporting worsening of symptoms and 10.6% reporting both improvement and worsening of certain symptoms. Killeen et al also reported specifically on cough headache in adults, a commonly used indication for surgery, and found that 37% reported an improvement, 51.9% no change and 11.1% worsening of headaches. Twenty-eight percent of migrainous headache symptoms were also reported to have improved, but little other information was provided on migraine or other symptoms in the adult cohort.[5]

Similarly, Chavez et al. found that 47.1% of adult patients improved (mean follow up of 15.2 months, standard deviation of 23.5 months), with the likelihood of improvement being affected by the presenting symptoms of the patient. This allowed the stratification of patients by their likelihood of improvement with conservative management. 88.9% of patients presenting with nausea improved at follow-up and the remaining 11.1% remained unchanged; 61.5% of migrainous headaches improved and 31.3% were unchanged. Whilst other symptoms improved less frequently, paraesthesia and ataxia either improved or remained the same in 75.4% and 82.1% of patients respectively. Whilst symptoms of nausea improved less frequently in the surgical management group (85.7%) than with conservative management, most symptoms improved more frequently with surgical intervention; cough headaches (94.6%), migraine headaches (92.9%), ataxia (87.5%).[4]

Outwith these two studies there are additional infrequent case reports of spontaneous resolution of malformations including associated syringomyelia.[6, 10]

Whilst many patients did well with conservative management, some patients did report deterioration of symptoms. Chavez et al. reported that 11.8% of the patients under conservative management developed new symptoms over the follow-up period, such as diffuse headaches, numbness and dysphagia.[4] Killeen et al. reported that 25.5% of conservatively managed adult

patients reported worsening of symptoms.[5] There are some reports of severe and life-threatening presentations in patients found to have CM-1, such as with acute respiratory failure[8] and sleep related breathing disorders.[7] These severe presentations appear to be rare, however, and are not described in larger studies.

Specific subpopulations of patients may have more adverse outcomes than expected. McDonnell et al looked at CM-1 in patients with spina bifida and reported that 23.7% of this population reported new symptoms over the previous 12 months.[9]

There is some evidence to suggest that pediatric and adult patients with Chiari Malformation 1 have different outcomes. In comparison to the adult population, pediatric patients tended to be less symptomatic at diagnosis and have a higher likelihood of improvement at follow-up. In Killeen et al, pediatric patients reported improved or stable symptoms in 95.2% of cases compared to the 63.8% of adult patients (p<0.05). Killeen et al. demonstrated that this difference existed not only between pediatric and adult groups but that it was age dependent, with improvement of symptoms being predicted by younger age at presentation. The odds of improvement of symptoms were 0.48 times lower for every 10-year increase in age (95% CI 0.28–0.815, $p < 0.05$).[5] This has significant implications for research that combines both adult and pediatric patient groups without separating the two populations.

Natural history of Asymptomatic Chiari Malformation 1

Despite a prevalence of 0.24%, the long-term prognosis of *asymptomatic* CM-1 has been poorly studied.[11] In the literature search we initially identified one paper, Bindal et al., which followed 27 patients over several years with CM-1.[3] Of these there were only five patients who were asymptomatic and who did not have surgery. It was found that after a mean 2-year follow-up, all five remained asymptomatic.

We identified two additional papers that reported asymptomatic CM-1 patients over a period of several years. Nishizawa et al identified nine patients with asymptomatic CM-1 and syringomyelia who were monitored for more than 10 years. All patients had presented incidentally during brain "check-ups", head injuries, tension headaches or paranasal sinusitis. In

the follow-up period of 11.2 years (+/-0.7), Eight patients remained asymptomatic and showed no neurological change. One patient noticed clumsiness of fingers 7 years after diagnosis and underwent surgery with a successful outcome. Additionally, there were no significant differences in the MRI scan findings over the 10 year period, including the patient who had surgery, up until the time of the operation.[15]

Santoro et al. also reported an asymptomatic case of CM-1 and syringomyelia incidentally diagnosed in a pregnant woman. Five years later, when presenting to the hospital with pregnancy for the second time, the same patient underwent an MRI which showed the presence of CM-1 without syringomyelia. The patient remained asymptomatic throughout this time.[16]

Coexistence of Syringomyelia with Chiari Malformation 1

Syringomyelia commonly coexists with CM-1, being present in around 50% of cases.[13] The presence of a syrinx has been repeatedly advocated as an indicator for surgical intervention[12,13] and indeed Chavez et al found that patients treated surgically were more likely to have a coexistent syrinx ($p<0.0001$).[4] There is limited evidence to substantiate this position, particularly in light of the fact that patients with coexistent syringomyelia are rarely studied separately from those with CM-1 alone. The presence of a coexistent syrinx has however been reported as a negative predictor of improvement after surgical decompression.[13, 14]

There is some evidence to suggest that conservative management is appropriate in patients with coexistent syringomyelia who are asymptomatic at diagnosis. Nishizawa et al. found that most of these patients showed no neurological change over long-term follow-up (mean 11.2 years), suggesting that if patients are asymptomatic then conservative management is appropriate. However, only nine patients were in this group in their study, of which one exhibited neurological changes after 7 years of follow-up, and underwent surgical intervention.[15] As sudden deterioration has been observed in patients with previously asymptomatic syringomyelia,[17] careful long-term monitoring would be prudent.

Discussion

There were no randomized controlled trials of surgery versus conservative management of CM-1. The best published evidence was level 2a and 2b cohort or case comparison series. It is therefore possible to suggest grade B recommendations for the management of symptomatic adult CM-1.

Patients presenting with significant headaches, ataxia or paresthesia are more likely to undergo surgical treatment of CM-1, although the decision to operate is a subjective one, depending on the balance of severity of symptoms, impact on quality of life, and the potential for surgical complications. In the absence of symptoms, there is little evidence to suggest that surgery should be performed on the basis of radiological findings alone.

If patients are mildly symptomatic, CM-1 is not necessarily a progressive condition and mild symptoms may remain static or improve with time. Therefore it is reasonable to observe patients who present with mild symptoms, although there are rare case reports of sudden deterioration. It is not possible to determine risk factors for sudden deterioration from the evidence available, and this should be placed into context when discussing the management of CM-1 with patients in the clinic. Surgery should be offered if symptoms subsequently deteriorate.

When patients present with asymptomatic CM-1, the majority of these patients are likely to remain asymptomatic. The larger studies show that very few asymptomatic patients require surgery over 10 years after diagnosis. The presence of a large syrinx can sometimes be alarming at first presentation, and many surgeons may advocate surgery in case of progression. However, it is not uncommon for patients to present with very few or mild symptoms despite a large syrinx, and again it is reasonable to observe such patients and offer surgery if the severity of symptoms warrants surgical intervention in the future, or there is significant radiological progression of the syrinx. However, due to the low number of asymptomatic patients in these studies the recommendations for management of asymptomatic patients is weaker (grade C).

After surgery, symptoms of headache and ataxia are most likely to improve, but other symptoms may not, even within the same patient. Symptoms of nausea and non-specific symptoms are less

likely to improve.

Potential risks of surgery include meningitis (4.8%), wound infection (3.2%), stroke (0.7%)[32] hydrocephalus (3.0%) and CSF fistula (5.9%).[33] This should be weighed against the potential benefits of surgery, which vary with operative technique[34] and the severity of symptoms, accepting that most patients follow an indolent course and some patients with mild symptoms may actually improve.

Limitations of the review

There are very few studies with large numbers of patients, and all are retrospective non-randomized studies, providing level 2 evidence at best. Therefore the strength of recommendation is limited to grade B for the management of symptomatic adult CM-1 patients. For asymptomatic adult CM-1 patients, whilst the available evidence portrays a fairly benign course over long-term follow up, the number of patients in these studies limits recommendations to grade C.

There is also likely to be selection bias when retrospectively comparing surgical and conservative cohorts in the literature, as surgical patients may have more severe symptoms.

Recommendations

The key limiting factor for further advancement of management recommendations in asymptomatic and symptomatic adult CM-1 patients is the size and retrospective nature of much of the currently available evidence. The development of a registry for such patients, thus allowing aggregation and long-term follow up would be of significant benefit.

Conclusions

The natural history of symptomatic and asymptomatic CM-1 in adults is relatively benign and non-progressive, therefore the decision to perform a foramen magnum decompression operation should be based on the severity and duration of a patient's symptoms at the time of presentation. It is reasonable to observe a patient with mild or asymptomatic symptoms, even in the presence of significant tonsillar descent or syringomyelia. Although class 1 evidence is lacking, there is sufficient evidence to suggest that randomizing patients into a surgical arm of a clinical trial would not be reasonable if they were mildly symptomatic or asymptomatic, and patients should be offered surgery dependent on the severity of presenting symptoms.

Patients with CM-1 who are either asymptomatic or mildly symptomatic at diagnosis may improve or remain symptomatically stable with conservative management. Whilst serious deterioration has been reported, this is rare and must be balanced against the known risks of surgical intervention.

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