REVIEW ARTICLE

Severe Cerebellar Degeneration and Chiari I Malformation - Speculative pathophysiology based on a systematic review

Andrei Fernandes Joaquim[1]

1. Professor de Neurocirurgia - Universidade de Campinas (UNICAMP), Campinas-SP

http://dx.doi.org/10.1590/1806-9282.66.3.375

SUMMARY

BACKGROUND: *Symptomatic Chiari Type I Malformation (CM) is treated with posterior fossa decompression with or without duroplasty. We have noticed some cases with concomitant severe cerebellar ataxia due to cerebellar atrophy. The aim of this study is to review the literature of CM associated with severe cerebellar atrophy and discuss its potential physiopathology.*

METHODS: *A systematic literature review in the Pubmed Database was performed using the following key-terms: "cerebellar atrophy Chiari", and "cerebellar degeneration Chiari". Articles reporting the presence of cerebellar degeneration/atrophy associated with CM were included.*

RESULTS: *We found only six studies directly discussing the association of cerebellar atrophy with CM, with a total of seven cases. We added one case of our own practice for additional discussion. Only speculative causes were described to justify cerebellar atrophy. The potential causes of cerebellar atrophy were diffuse cerebellar ischemia from chronic compression of small vessels (the most mentioned speculative cause), chronic raised intracranial pressure due to CSF block, chronic venous hypertension, and association with platybasia with ventral compression of the brainstem resulting in injury of the inferior olivary nuclei leading to mutual trophic effects in the cerebellum. Additionally, it is not impossible to rule out a degenerative cause for cerebellar atrophy without a causative reason.*

CONCLUSIONS: *Severe cerebellar atrophy is found in some patients with CM. Although chronic ischemia due to compression is the most presumed cause, other etiologies were proposed. The real reasons for cerebellar degeneration are not known. Further studies are necessary.*

KEYWORDS: *Arnold-Chiari Malformation. Cerebellum/abnormalities. Cerebellar diseases. Systematic review.*

INTRODUCTION

Chiari malformation (CM) is characterized by a congenital malformation of the posterior cranial fossa with cerebellar tonsils herniation through the foramen magnum, probably due to the underdevelopment of the posterior bony skeleton (exo-occipital and supraoccipital bones)[1,2]. Symptoms may have a wide range of clinical presentations, such as motor and sensory deficits, cranial nerve palsies, as well as cerebellar symptoms (ataxia, dysmetria, among others)[1-4]. When symptomatic, surgical treatment is well accepted, consisting of posterior fossa decompression, with or without duroplasty[1-4].

In our clinical experience, we have noticed that some patients present severe cerebellar ataxia, even after surgical treatment, due to severe atrophy, with cerebellar substance degeneration. The aim of this study is to review the potential causes of cerebellar atrophy in patients with symptomatic CM, before or even after surgical treatment.

DATE OF SUBMISSION: 01-Sep-2019
DATE OF ACCEPTANCE: 10-Oct-2019
CORRESPONDING AUTHOR: Andrei Fernandes Joaquim
Cidade Universitária Zeferino Vaz, Campinas, SP, Brasil - 13090-610
E-mail: andjoaquim@yahoo.com

METHODS

In an attempt to study the relationship between cerebellar atrophy and CM, two electronic searches were conducted on PubMed (MEDLINE) in July 2019. We used the following search terms: "cerebellar atrophy Chiari" obtaining 40 articles titles. Another search was performed using the following search terms: "cerebellar degeneration Chiari" obtaining 16 titles. From the 56 revised titles with their respective abstracts, four case reports were included from the first search and two from the second one, with a total of six articles reporting cerebellar degeneration associated with CM. An illustrative case treated by the author was also included.

Since only case reports were evaluated, our review was classified by the Oxford Centre of Evidence-Based Medicine[5] as evidence level 4 (case series of poor quality).

RESULTS

We found six studies in our literature search, all of which were case reports, with a total of seven patients discussed (one case report had two illustrative cases)[6-11]. They were all described in detail. The majority of the authors rule out other causes of cerebellar degeneration, such as infections, inflammatory diseases, and medications/drugs.

Gebarski and Greenberg[6] reported the first case, in the CT scan era, (1984) of loss of cerebellar substance in a patient with CM. A 40-year-old woman with gait instability and visual blurring was diagnosed with olivopontocerebellar degeneration. She underwent clivomyelography with iophendylate demonstrating herniation of the cerebellar tonsils to the level of the axis. She also had a cerebral angiography demonstrating displacement of the tonsillohemispheric branches of the posterior inferior cerebellar arteries (PICA). She then underwent a suboccipital craniectomy with laminectomy of C1 and C2 and dural grafting, reestablishing normal gait and vision two months after the surgery. Authors proposed that the diffuse cerebellar ischemia from chronic compression of the small vessels was the cause of loss of cerebellar substance, although no arterial occlusions were noted in the limits of the subtraction angiography and no supratentorial ischemia or atrophy was documented. They emphasized that the loss of cerebellar substance should not be considered evidence enough to exclude the diagnosis of CM.

Goel et al.[7], almost 18 years after the first description of the association of cerebellar atrophy and CM, reported two cases of Basilar Invagination (BI) associated with CM in patients with severe cerebellar atrophy. It was the first report in the MR era. The first patient was a 24-year-old woman with gait impairment in the previous three years, associated with hoarseness of voice, dysphagia, and nasal regurgitation. She also had BI with CM, atlas occipitalization, and marked atrophy of the cerebellum. Digital angiography showed a "bulbar hump" but a normal filling of all posterior cranial fossa blood vessels. One year after the surgery, there was a marked improvement in her speech, swallowing, and her gait was normal. The other patient was a 38year-old man with complaints of imbalance, vertigo, and difficulty in swallowing for one month. He also had an MR with CM and BI with assimilation of the atlas and severe cerebellar atrophy. The angiography showed normal filling of posterior circulation with some stretching of the PICA. After bone decompression at the posterior fossa, marked improvement was reported. The authors reported that both patients did not have cerebral atrophy. Explanations included continuous insufficiency of blood supply to the brainstem and cerebellum, once infarction was not plausible due to the normal angiography exam. Interestingly, in both cases, there were marked BI with platybasia and a concavity of the brainstem, with normal tonsils morphology in an abnormal cerebellum.

Kempster and Pullar[8], in 2003, published a letter about the publication of Goel et al.[7]. In it, they also reported a 57-year-old man who had severe gait complaints, as well as speech slurring and swallowing difficulties. Although they did not publish images, the description of the MR reported a marked indented ventral surface of the upper medulla without signs of cerebellar or brainstem infarction and a dolicho-ectatic left vertebral artery. The cerebellar atrophy was more evident in the vermis. They proposed that a potential mechanism of cerebellar atrophy was due to some sort of trans-synaptic neuronal degeneration – with ventral compression at the level of the inferior olivary nuclei, a major source of cerebellar afferents, which resulted in trophic effects in the cerebellum due to the connections with the cerebellar Purkinje cells. Damage to one group of these neurons potentially may lead to degeneration of the others, according to animal studies (in rats).

Maurya and Singh[9], in 2003, reported a 34-year-old man with the diagnosis of cerebellar degeneration

from a CT scan, who subsequently had a diagnosis of CM after an MR. The patient had had gait unbalance in the previous three years, mild dysarthria with normal motor and sensory system exams. There was downbeat nystagmus, which was associated with cervicomedullary junction diseases. The CT showed marked cerebellar atrophy with asymmetry (the left side was more affected than the right one). Then, the MR showed tonsillar herniation below the foramen magnum without syringomyelia. Although the MR did not show any evidence of acute or subacute ischemic brain injury, they also speculated that diffuse cerebellar ischemia from chronic compression was the cause of cerebellar atrophy. The authors proposed that CM should be considered as a differential diagnosis of loss of cerebellar substance.

Petracca et al.[10], in 2013, reported a 33-year-old woman who had had previous surgery (posterior fossa decompression) for CM with complete resolution of tonsillar herniation in an early postoperative MR, with an improvement of sensory symptoms and also some improvement in walking unsteadiness. Three years after the surgery, she returned with symptoms of a cerebellar syndrome (imbalance and speech impairment), dysphagia, diplopia, and dizziness. She also had scanning speech, gait instability, and nystagmus in all gaze directions, with bilateral dysmetria. A screening for ataxia was performed and also a neurophysiological study of the upper and lower limbs with analysis of sensory and motor conduction, with axonal neuropathy. A new MR was performed about six years after the first one, with a diagnosis of severe cerebellar atrophy and late-onset idiopathic cerebellar ataxia (ILOCA). ILOCA is characterized by a neurodegenerative disorder of adult-onset and unknown cause of progressive cerebellar ataxia and atrophy of the cerebellum (and sometimes, also the brainstem). The authors proposed that ILOCA did not seem to be linked to CM.

Moscote-Salazar et al.[11] reported the case of an 18-year-old woman with headaches in the previous six months, with an associated quadriparesis. An MR showed tonsillar herniation and syringomyelia. She underwent posterior fossa decompression with a laminectomy of C1 and had fully recovered from her symptoms after three years of follow-up. In the same MR, severe cerebellar atrophy was evident. No mechanism to explain the cerebellar changes were proposed by the authors.

We also added the illustrative case of a 58-year-old man with CM surgically treated with posterior fossa decompression ten years ago who had later worsening of cerebellar ataxia with severe cerebellar atrophy (Figure 1). This patient had severe ataxia, almost unable to walk (requires flares), severe dysarthria, and dysmetria, but did not have pain or motor symptoms. He did not undergo another surgical procedure once his symptoms were attributed to severe cerebellar degeneration. A BI secondary to clivus hypoplasia and some ventral brainstem compression was evident.

DISCUSSION

Since the first paper about cerebellar ectopia published by Hans Chiari in 1891, congenital

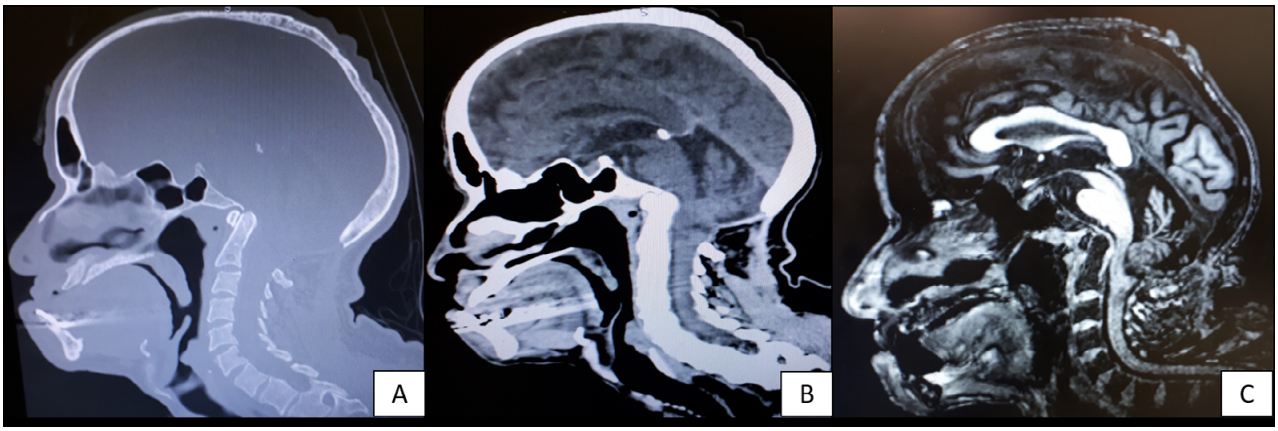

FIGURE 1. A) SAGITTAL BONE CT SCAN SHOWING CLIVUS HYPOPLASIA, PLATYBASIA, AND A POSTERIOR FOSSA DECOMPRESSION WITH A C1 LAMINECTOMY. B) SAGITTAL SOFT TISSUE CT SCAN SHOWING SOME VENTRAL COMPRESSION OF THE MEDULLA BY THE CLIVUS AND CEREBELLAR ATROPHY. C) SAGITTAL T1 MRI WITH SEVERE CEREBELLAR ATROPHY. ONCE THE PATIENT HAD ONLY ATAXIA ATTRIBUTED TO THE CEREBELLAR DEGENERATION, WE DID NOT INDICATE A NEW SURGICAL PROCEDURE.

craniocervical junction anomalies are still full of controversies[2,12]. The many different radiological presentations, which may include osseous components of the dysgenesis, such as atlantoaxial instability, BI, Klippel-Feil anomalies, atlas occipitalization, scoliosis, facet joints malformations, tethering cord, among many others, are extensively discussed in the literature[1,2,13-19]. When considering the neural components of CM, the association of CM with hydrocephalus, syringomyelia, and syringobulbia is also extensively found[13]. However, cerebellar atrophy has rarely been described, although we have noticed that this finding is not so rare.

In our review, we only found six studies discussing cerebellar atrophy associated with CM, with a total of seven patients, or eight patients, including our additional case. The images of the first case, date from 1984, and it is not possible to clearly elucidate if there is concomitant BI in the axial CT scan[6]. The two cases presented by Goel et al.[7] had severe BI with ventral brainstem compression. The fourth case, presented by Kempster and Pullar[8], did not have MR images available, but the authors reported that the patient had severe anterior brainstem compression without signs of cerebellar infarction. The fifth case reported by Maurya et al.[9] had only CM, without an evident BI and without ventral compression. The sixth case reported by Petracca et al.[10] also did not have evident BI. The seventh case reported by Moscote-Salazar et al.[11] had CM with important ventral brainstem compression, similarly to our illustrative case. Considering the eight cases reviewed, only two were "pure" CM, five had also BI with ventral brainstem compression, and one was inconclusive. It means that although ventral brainstem compression may play an important role in the development of cerebellar atrophy, it cannot be the only explanation for this finding.

The normal vascular flow documented in angiography of the posterior fossa performed in the cases of Gebarski and Greenberg[6], as well as in the Goel et al.[7] cases, suggested that infarction was not the reason for cerebellar atrophy, although the authors postulated that continuous insufficient blood supply might play a role in the physiopathology of cerebellar degeneration.

The theory proposed by Kempster et al.[8], based on animal studies (rats), that damage to the inferior olivary neurons may result in atrophy in the cerebellar Purkinje cells due to mutual trophic effects may be considered in cases with ventral brainstem compression[20]. However, as explained above, two patients had "pure" CM, without ventral brainstem compression in published images. For this reason, this explanation may also be questioned or does not explain atrophy in all cases.

Ito et al.[21] described a case of a 50-year-old woman who had a 40-year history of progressive sensorimotor deficits with CM with severe spinal cord atrophy below C12 (in the cervical, thoracic and lumbar spine, without tethering). She underwent foramen magnum decompression and C1 laminectomy with duraplasty, with progressive improvement. The authors speculated that spinal cord atrophy might be due to secondary retention of CSF at the spinal canal or spontaneous resolution of syringomyelia. We may also infer that CSF obstruction in the foramen magnum plays a role in cerebellar atrophy – with compartmental posterior fossa hypertension, the cerebellar tissue may be more sensitive to the higher pressure and degenerates. This local hypertension may result in direct compression of the cerebellum tissue in the bone of the posterior fossa – another potential mechanism of atrophy. This theory may be justified by venous hypertension and poor drainage of the posterior fossa in some patients with CM. We have observed some patients with severe BI with clivus hypoplasia that had important sinus bleeding when the dura of the posterior fossa was opened in decompressive procedures. To corroborate this theory, Saindane et al.[22] evaluated the severity of transverse sinus stenosis in contrast-enhanced brain MRIs of 30 patients who had surgery for CM and compared the findings with 76 controls subjects. Two different readers blinded to the diagnosis reported that CM patients had a higher rate of unilateral than bilateral transverse sinus stenosis. This finding may reflect associated intracranial hypertension due to an obstruction of the CSF flow or even poor venous drainage.

The main limitation of our study is the sparse literature about the association of cerebellar atrophy and CM. Additionally, we should also emphasize that many patients with CM may have some degree of cerebellar substance atrophy but did not present any symptoms related to it. However, this is the first study to review this problem and has raised many potential causes for cerebellar atrophy. Further studies are necessary to elucidate better the reasons for cerebellar degeneration in some patients with CM.

CONCLUSIONS

Although not common, severe cerebellar atrophy is found in some patients with CM, more commonly with associated BI. Many potential causes could justify this association, such as chronic ischemia, ventral brainstem compression, CSF hypertension, venous hypertension, or even an intrinsic degeneration. However, the reason for cerebellar degeneration in some patients with CM is not known. Further studies are necessary.

RESUMO

OBJETIVO: *A Malformação de Chiari (MC) tipo I sintomática é tratada através da descompressão da fossa posterior com ou sem duroplastia. Observamos alguns casos com ataxia cerebelar grave concomitante devido à atrofia cerebelar. O objetivo deste estudo é revisar a literatura sobre MC associada à atrofia cerebelar grave e discutir sua possível fisiopatologia.*

METODOLOGIA: *Conduzimos uma revisão sistemática da literatura no banco de dados Pubmed utilizando as seguintes palavras-chave: "cerebellar atrophy Chiari", e "cerebellar degeneration Chiari". Artigos sobre a presença de degeneração/atrofia cerebelar associada à MC foram incluídos.*

RESULTADOS: *Encontramos apenas seis estudos que discutiam diretamente a associação entre atrofia cerebelar e MC, com um total de sete casos. Nós adicionamos um caso da nossa própria prática para ampliar a discussão. Apenas causas especulativas foram descritas para justificar a atrofia cerebelar, entre elas: isquemia cerebelar difusa devido à compressão crônica de pequenos vasos (a causa especulativa mais citada), pressão intracraniana elevada crônica devido ao bloqueio de LCR, hipertensão venosa crônica e associação com platibasia com compressão ventral do tronco cerebral, resultando em lesão do núcleo olivar inferior e levando a efeitos tróficos mútuos no cerebelo. Além disso, não é possível descartar uma causa degenerativa para atrofia cerebelar sem motivos claros.*

CONCLUSÃO: *A atrofia cerebelar grave é encontrada em alguns pacientes com MC. A isquemia crônica causada por compressão é a causa mais apontada como suspeita, porém outras etiologias foram propostas. As reais causas da degeneração cerebelar não são conhecidas. Mais estudos são necessários.*

PALAVRAS-CHAVE: *Malformação de Arnold-Chiari. Cerebelo/anormalidades. Doenças*

REFERENCES

1. Joaquim AF, Fernandes YB, Mathias RN, Batista U, Ghizoni E, Tedeschi H, et al. Incidence of basilar invagination in patients with tonsillar herniation? A case control craniometrical study. Arq Neuropsiquiatr. 2014;72(9):706-11.
2. Joaquim AF, Tedeschi H, Chandra PS. Controversies in the surgical management of congenital craniocervical junction disorders: a critical review. Neurol India. 2018;66(4):1003-15.
3. Sabba MF, Renor BS, Ghizoni E, Tedeschi H, Joaquim AF. Posterior fossa decompression with duraplasty in Chiari surgery: a technical note. Rev Assoc Med Bras (1992). 2017;63(11):946-9.
4. Joaquim AF. Atlantoaxial instability and Chiari malformation. J Neurosurg Spine. 2015;22(5):559.
5. Oxford Centre of Evidence-Based Medicine. Levels of evidence and grades of recommendations. [cited 2019 Aug 3]. Available from: http://www.cebm.net/oxford-centre-evidence-based-medicine-levelsevidence-march-2009/
6. Gebarski SS, Greenberg HS. Chiari malformation presenting as loss of cerebellar substance on computed tomography. Surg Neurol. 1984;21(6):562-4.
7. Goel A, Desai K, Bhatjiwale M, Muzumdar DP. Basilar invagination and Chiari malformation associated with cerebellar atrophy: report of two treated cases. J Clin Neurosci. 2002;9(2):194-6.
8. Kempster PA, Pullar MJ. Re: Basilar invagination and Chiari malformation associated with cerebellar atrophy: report of two treated cases. J Clin Neurosci. 2003;10(3):394.
9. Maurya V, Singh H. Chiari malformation presenting as cerebellar degeneration. Med J Armed Forces India. 2003;59(2):147-8.
10. Petracca M, Cerillo I, Montenella S, Cerullo G, Carrieri PB. Idiopathic late-onset cerebellar ataxia with cerebellar atrophy in a patient diagnosed with Chiari I malformation: a case report. Neurol Sci. 2013;34(12):2235-7.
11. Moscote-Salazar LR, Calderón-Miranda WG, Alvis-Miranda HR, Lee-Aguirre Á, Alcalá-Cerra G. Type I Chiari malformation associated with cerebellar atrophy. Case report. Rev Med Inst Mex Seguro Soc. 2017;55(2):260-3.
12. Chiari H. Uber Veranderungendes kleinhirnsinfolge von hydrocephaliedes grosshirns. Dtsch Med Wochenshr 1891;17:1172-5.
13. Goel A. Basilar invagination, Chiari malformation, syringomyelia: a review. Neurol India. 2009;57(3):235-46.
14. Miranda CEV, Torres HHJ, Barreiro GC, Joaquim AF, Tedeschi H. Management of a complex basilar invagination case with multiple revision surgeries: case report. Arq Bras Neurocir. 2017;36(1):62-5.
15. Joaquim AF, Ghizoni E, Giacomini LA, Tedeschi H, Patel AA. Basilar invagination: surgical results. J Craniovertebr Junction Spine. 2014;5(2):78-84.
16. Joaquim AF, Ghizoni E, Almeida JP, Anderle DV, Tedeschi H. Basilar invagination secondary to hypoplasia of the clivus: is there indication for craniocervical fixation? Coluna/ Columna. 2014;13(1):69-70.
17. Steinmetz MP, Benzel EC. Surgical management of Chiari malformation. Neurosurg Quart. 2003;13(2):105-12.
18. Milhorat TH, Bolognese PA, Nishikawa M, Francomano CA, McDonnell NB, Roonprapunt C, et al. Association of Chiari malformation type I and tethered cord syndrome: preliminary results of sectioning filum terminale. Surg Neurol. 2009;72(1):20-35.
19. Silva OT, Ghizoni E, Tedeschi H, Joaquim AF. Role of dynamic computed tomography scans in patients with congenital craniovertebral junction malformations. World J Orthop. 2017;8(3):271-7.
20. Strata P, Tempia F, Zagrebelsky M, Rossi F. Reciprocal trophic interactions between climbing fibres and Purkinje cells in the rat cerebellum. Prog Brain Res. 1997;114:263-82.
21. Ito Y, Tsuboi K, Akutsu H, Ihara S, Matsumura A. Advanced Chiari malformation type 1 with marked spinal cord atrophy. Case report. J Neurosurg Spine. 2005;3(4):324-7.
22. Saindane AM, Bruce BB, Desai NK, Roller LA, Newman NJ, Biousse V. Transverse sinus stenosis in adult patients with Chiari malformation type I. AJR Am J Roentgenol. 2014;203(4):890-6.