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Subpial Aspirated Cerebellar Tonsils in Pediatric Chiari I Malformation: anatomopathological study

Tonsilas Cerebelares de Crianças com Malformação de Chiari Tipo I Submetidas a Aspiração Subpial. Estudo anatomopatológico

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ABSTRACT

Introduction: *Chiari Malformation (CM) is a condition in which ectopy or herniation of components of the posterior cranial fossa to the foramen magnum are present, and can be divided into four types. Type I (CM-I) occurs when there is protrusion of only the cerebellar tonsils into the cervical spinal canal. One of the available therapeutic options is subpial aspiration. Previous anatomopathological studies showed that the main alterations in the aspirated tonsils were the loss of Purkinje cells, Bergmann gliosis, cortical atrophy and neuronal changes due to hypoxia; all of them secondary to the aggression to the nervous tissue over time. These changes lead to gradual loss of function of the tissue, with compensation by other structures. Therefore, when subpial aspiration of the herniated tonsil is performed in adults, there are no negative consequences to the patient in the future, as concluded by many studies targeting adults with CM. However, studies in children with CM are scarce, which means that we cannot affirm in which age the histological changes occur. Hence, we cannot determine whether or not the surgical removal of this tissue in childhood leads to future losses to the patient.* ***Objective:*** *To analyze the main histological aspects of cerebellar tonsils in children with Chiari I Malformation who underwent subpial aspiration, to help clarify the natural history of this pathology, as well as to help determine the prognosis of this population when treated with this technique.* ***Method:*** *We analyzed the histopathology of the tonsils removed with subpial aspiration technique, in several hospitals of João Pessoa, Brazil, from children diagnosed with Chiari I malformation.* ***Results:*** *The slides of all tonsils showed the same histological changes: Bergmann gliosis, loss of Purkinje cells, atrophy of the cerebellar cortex and meningeal fibrosis. The obtained results were similar to the ones found in previous studies carried out in adults.* ***Conclusion:*** *The cerebellar anatomopathological alterations secondary to Chiari I Malformation, which leads to loss of tissue function, seem to appear early in life, suggesting the safety of the subpial aspiration in pediatric patients. However, more extensive studies and long-term follow-up of patients are needed to establish with more precision the natural history of the disease.*

Keywords: *Arnold-Chiari Malformation; Neurosurgery; Pathology; Surgical; Gliosis*

RESUMO

Introdução: *Malformação de Chiari (MC) é uma condição na qual existe ectopia ou herniação de componentes da fossa posterior do crânio para o forame magno. Pode ser dividida em quatro tipos. O tipo I ocorre quando há protusão apenas das tonsilas cerebelares para dentro do canal vertebral. Uma das opções terapêuticas disponíveis é a aspiração subpial. Estudos anatomopatológicos já realizados mostraram que as principais alterações das tonsilas aspiradas foram perda das células de Purkinje, gliose de Bergmann, atrofia cortical e alterações neuronais por hipóxia, todas secundárias à agressão ao sistema nervoso ocorrida com o passar do tempo. Essas mudanças levam à gradual perda de função do tecido, com compensação por outras estruturas. Portanto, quando é realizada aspiração subpial das tonsilas herniadas em adultos, não há consequências negativas ao paciente no futuro, como já concluído por muitos estudos com adultos portadores de MC. Entretanto, estudos com crianças são escassos, o que significa que não se sabe ao certo a partir de que idade as referidas alterações histológicas acontecem. Assim, não é possível determinar se a remoção cirúrgica desse tecido na infância traz prejuízos futuros ao paciente.* ***Objetivo:*** *Analisar os principais aspectos histológicos de tonsilas cerebelares de crianças com Malformação de Chiari Tipo I (MC I) submetidas à aspiração subpial. Com isso, espera-se contribuir para a compreensão da história natural da doença, bem como determinar o prognóstico da população pediátrica quando tratada com essa técnica.* ***Materiais e métodos:*** *Foram analisados os laudos anatomopatológicos das lâminas de tonsilas removidas pela técnica de aspiração subpial em diferentes hospitais de João Pessoa, Brasil, de cinco crianças diagnosticadas com MC I. Os resultados encontrados foram*

comparados ao observado em adultos. ***Resultados:*** *Todas as lâminas analisadas apresentaram alterações histológicas semelhantes: gliose de Bergmann, perda de células de Purkinje e atrofia do córtex cerebelar.* ***Discussão:*** *Os resultados obtidos foram similares ao de estudos realizados previamente com adultos.* ***Conclusão:*** *As alterações na histologia cerebelar secundárias à MC I parecem ter início em fases iniciais da vida, o que sugere segurança da aspiração subpial em crianças. Entretanto, estudos de maior impacto com seguimento de longo prazo dos pacientes são necessários para estabelecer com maior precisão a história natural da doença.*

Palavras-chave: *Malformação de Chiari; Neurocirurgia; Patologia; Cirurgia; Gliose*

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INTRODUCTION

Chiari Malformation (CM) is a condition in which there is ectopy or herniation of components of the posterior cranial fossa to the foramen magnum[1]. It can be divided in four types, based upon the degree of anatomical abnormalities found: Type I (CM-I), when there is protrusion of only the cerebellar tonsils into the cervical spinal canal; Type II (CM-II), characterised by cerebellar vermis herniation in addition to the inferior portion of the brainstem into the spinal canal; Type III (CM-III), presenting the same type II characteristics along with occipitocervical encephalocele; Type IV (CM-IV), described as severe hypoplasia or aplasia of the cerebellum, associated with a small posterior cranial fossa[2].

The most evident symptomatology in this disease is headache, usually located in the occipital and neck region, worsened by maneuvers such as Valsalva, coughing or sneezing. Cervicalgia, neck stiffness, diplopia and vertigo are also reported, mainly due to compressive effects of the herniated material in the region[3].

Although the pathophysiology of CM in adults is well-understood, the treatment is perhaps one of the most controversial topics in neurosurgery[4]. Among the available therapeutic options, there is subpial aspiration, which consists of incising and aspirating the contents of the tonsils after opening and dissecting the dura mater in the posterior cranial foss [5].

Several anatomopathological studies have already been done with the aspirated material of patients who underwent subpial aspiration, such as the ones made by Pueyrredon et al. and Koga et al. [6]. Main alterations were shown to be loss of Purkinje cells, Bergmann gliosis, cortical atrophy and neuronal changes due to hypoxia. Also, studies have shown no correlation between histological changes and the size of tonsil herniation in adults [7,8].

The cellular alterations above mentioned are secondary to the aggression to the nervous tissue over time, whether ischemic or traumatic. These changes lead to gradual loss of function of the tissue, with compensation by other structures. Therefore, when subpial aspiration of the herniated tonsil is performed in adults, there are no negative consequences to the patient in the future, as concluded by many studies targeting adults with CM [9,10].

However, studies in children with CM are scarce, which means that we cnnot affirm in which age the histological changes occur. Hence, we cannot determine whether or not the surgical removal of this tissue in childhood brings future losses to the patient [7].

Thus, the present research aimed to assess the main histological aspects of tonsils in pediatric patients with Type I (CM-I) who underwent subpial aspiration, in order to help determine the prognosis of this population.

METHODS

We performed a cross-sectional, observational and quantitative study to assess the main anatomopathological aspects of tonsils in pediatric patients with Type I (CM-I) who underwent subpial aspiration.

Data was collected through review of medical records and anatomopathological reports of patients submitted to surgical correction of malformation of the craniovertebral junction, from 1994 to 2017, at several hospitals from João Pessoa, Brazil.

As inclusion criteria were used patients diagnosed with Type I (CM-I) by clinical aspects and evaluation by Magnetic Resonance Imaging (MRI), who were submitted to decompressive surgery by one of the authors, between 1994 and 2017, at the following hospitals: Senator Humberto Lucena Emergency and Trauma State Hospital, Alberto Urquiza Wanderley Hospital, Samaritano Hospital, São Francisco Memorial Hospital and Santa Isabel General Hospital, all located in João Pessoa, state of Paraíba, Brazil. Patients aged over 12 years; patients whose medical file lacked all the information necessary for this research and patients with clinical history of other pathologies in the central nervous system were excluded from the research.

The biopsied material was removed by subpial aspiration and sent to the appropriate anatomopathological analysis.

The study was based on secondary data, providing privacy and confidentiality, and was performed in agreement with the Resolution 466/12 of the National Health Council (Brazil), which addresses ethical aspects of research in humans. The present study was submitted to the Lauro Wanderley University Hospital Ethics Committee and approved under CAAE: 59415616.0.0000.5188.

RESULTS

After applying the inclusion criteria 65 patients were found, resulting in five after the exclusion criteria. The final sample was, then, composed by 5 children, aged between 6 and 12 years, 3 males and 2 females.

The slides of the 5 tonsils analyzed by light microscopy showed histological changes. The most striking alterations found in all analyzed pieces were Bergmann gliosis, the loss of Purkinje cells and atrophy of the cerebellar cortex. It was also observed meningeal fibrosis.

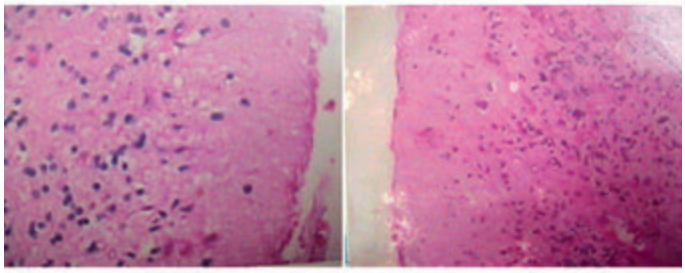

Figure 1. Sclerotic fragments of pediatric cerebellar tonsils showing loss of Purkinje cells.

DISCUSSION

The obtained results were practically identical to the ones found in studies carried out previously in adults, and confirmed the alterations demonstrated by Koga et al.[6] and Pueyrredon et al.[10]. Our research, however, showed the findings in cerebellar tonsils of children with no other alteration than Type I (CM-I). They were also similar to results found in the cohort study performed by Tubbs et al., in which children with Type I (CM-I) and cystic or ischemic alterations of the tonsils were analyzed [15].

Thus, through our analysis, we can infer that degenerative changes at cellular level in the herniated tonsil of patients with Type I (CM-I) have been present since childhood.

Among all the histological changes shown in our study and in the ones previously published, we had noticed two pathological situations: hypoxia or trauma. Thus, the most accepted theory to explain what occur at the cellular level in the herniated tonsils is that they are secondary to afferent arterial compression by the herniated tissue in the vertebral canal [9,10]. Another equally plausible explanation is the one that associates the changes to the trauma resulting from the passage of cerebrospinal fluid into a space compressed over time [9, 12].

Purkinje cells, for example, are notoriously sensitive to devascularization and ischemia. Since the patients here analyzed did not have a clinical history of other ischemic pathologies in the central nervous system, we can associate this alteration with chronic tonsillar compression, as described by Welsh, in 2002 [11].

One of the theories proposed to explain this degeneration of Purkinje cells is the decreased ability of these cells to store glutamate, leading to difficult generation of energy in situations of hypoxia [10]. It is also suggested that there is deficiency of aldolase C and EAT 4, which exacerbates the suffering of these cells against the excess of synaptic impulses of the inferior olivary nucleus [13]. On the other hand, Allen described Bergmann gliosis findings and loss of Purkinje cells in mild to moderate trauma situations[14].

Bergmann gliosis is well established in the literature as a result of any hypoxia process, and is also seen in patients with iron deficiency anemia. In the case of patients with CM, it is observed that this cellular proliferation leads to the formation of avascular cysts in the tonsil, macroscopic whitish [15].

It should be noted that, in children, the diagnosis is made difficult by the lack of alterations in the physical neurological examination[16]. As few cases are diagnosed, there is a small number of long-term evolution descriptions and of anatomopathological aspects of biopsied tonsils [15].

CONCLUSION

All children with aspirated tonsils had anatomopathological abnormalities, the most common were Purkinje cell loss and Bergmann gliosis, results that are similar to those already published in adults. Such findings suggest that cerebellar anatomopathological alterations secondary to Type I (CM-I) appear early in life. However, more extensive studies and long-term follow-up of patients are needed to establish with more precision the natural history of the disease and the safety of subpial aspiration in pediatric patients.

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