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ORIGINAL PAPER

Histological findings in cerebellar tonsils of patients with Chiari type I malformation

Francisco Pueyrredon · Natalia Spaho · Ivonne Arroyave · Harry Vinters · Jorge Lazareff

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Abstract
Objectives Cerebellar tonsillectomy is often performed for relief of symptoms associated with Chiari type I malformation (CMI). Nonetheless, the idea of removing supposedly healthy central nervous tissue has been a source of concern for neurosurgeons. The aim of this paper is to determine the histological changes in the cerebellar tonsils of patients with a wide range of symptoms and conditions related to CMI.
Materials and methods The cerebellar tonsils of 43 pediatric patients with CMI were sent to pathology for histological examination.
Conclusion The cerebellar tonsils in a great majority of CMI patients can be abnormal. We suggest that the reported histological findings are secondary to injury and ischemia.

Keywords Arnold Chiari malformation · Cerebellar disease · Ischemia · Purkinje cell · Treatment · Tonsillectomy

Abbreviations

CMI	Chiari I malformation
CNS	central nervous system
PCL	Purkinje cell loss

F. Pueyrredon · N. Spaho · I. Arroyave · J. Lazareff (✉)
Division of Neurosurgery, Pediatric Neurosurgery,
David Geffen UCLA School of Medicine,
P.O. Box 957039, Los Angeles, CA 90095-7039, USA
e-mail: jlazareff@mednet.ucla.edu

H. Vinters
Division of Surgical Pathology, David Geffen University
of California at Los Angeles (UCLA) School of Medicine,
Los Angeles, CA, USA

Introduction

Chiari type I malformation (CMI) is a disorder defined by caudal displacement of the cerebellar tonsils through the foramen magnum into the cervical canal. Although hypotheses on the pathogenesis vary, the most widely accepted theory is a disorder of the para-axial mesoderm that is characterized by underdevelopment of the posterior cranial fossa and overcrowding of the normally developed hindbrain [10]. This implies that CMI is not a primary alteration of the central nervous system (CNS). The common denominator of the surgical procedures for alleviating CMI symptoms is to expand the volume of the posterior fossa and the upper cervical canal. This is achieved through several different techniques. Some perform only bone posterior fossa decompression [3], others bone decompression with duroplasty [9], and some perform cerebellar tonsillectomy [4, 6].

Koga et al. [5] have described that the cerebellar tonsils in Chiari patients were abnormal. Their valuable contribution was limited to five patients and all of them had syringomyelia. To determine if such alterations could be found in a broader range of patients, we conducted the study that we here report.

Materials and methods

Forty-three patients (22 men, 21 female), ranging in age from 4 months to 20 years, with an average of 8.6 years and median of 8 years, were studied.

Two patients had longstanding lumboperitoneal shunt, one for treatment of communicating hydrocephalus and the other for the treatment of an arachnoid cyst. In two children, the CMI was secondary to craniosynostosis,

while one had anterior plagiocephaly and the other brachycephaly.

All patients presented with symptoms and signs associated with CMI, most commonly headache, mainly occipital. Ataxia, vision loss, nausea and vomiting, retro-ocular pain, syncope, and scoliosis were also reported.

All patients underwent magnetic resonance imaging for the brain and spine, which revealed cerebellar tonsil displacement into the cervical canal in all of them. Nine patients developed syringomyelia.

During surgery, the atlanto-occipital space was exposed. Under microscopic magnification, we performed a cruciform incision in the dura mater. We then visualized the underlying cerebellar tonsils, grasped them with a forceps, cauterized its base, and resected them. The tissue obtained at surgery was sent for pathological examinations. After achieving the objectives of the procedure, we proceeded to close the wound using a synthetic dura mater [6].

Results

Of the 43 samples, 38 had histological alterations, and 5 were normal.

In 32 samples, we observed Purkinje cell loss (PCL). In 29 of these samples, the PCL was associated, in decreasing order of frequency, with Bergman gliosis, atrophic cerebellar cortex, meningeal fibrosis, and internal granular layer loss.

In six samples, the predominant histological alterations were gliosis with occasional Rosenthal fibers, fibrosis, cerebellar atrophy, focal degenerative changes, and anoxic neuronal changes.

Scattered eosinophilic neuronal changes were observed in both groups.

Both patients with the acquired CMI from the lumboperitoneal shunts had PCL and Bergman gliosis. There was no difference in histology between patients with tonsils that descended to the level of C-1 and those with tonsils descended to level C-2.

The nine patients who presented with syringomyelia had the following histology: five had PCL with gliosis, two were normal, one had significant cerebellar atrophy, and one had diffuse gliosis.

The five patients whose sampled cerebellar tonsils were normal had no common clinical or radiological pattern. Figure 1 illustrates PCL and contrasts it with normal cerebellum.

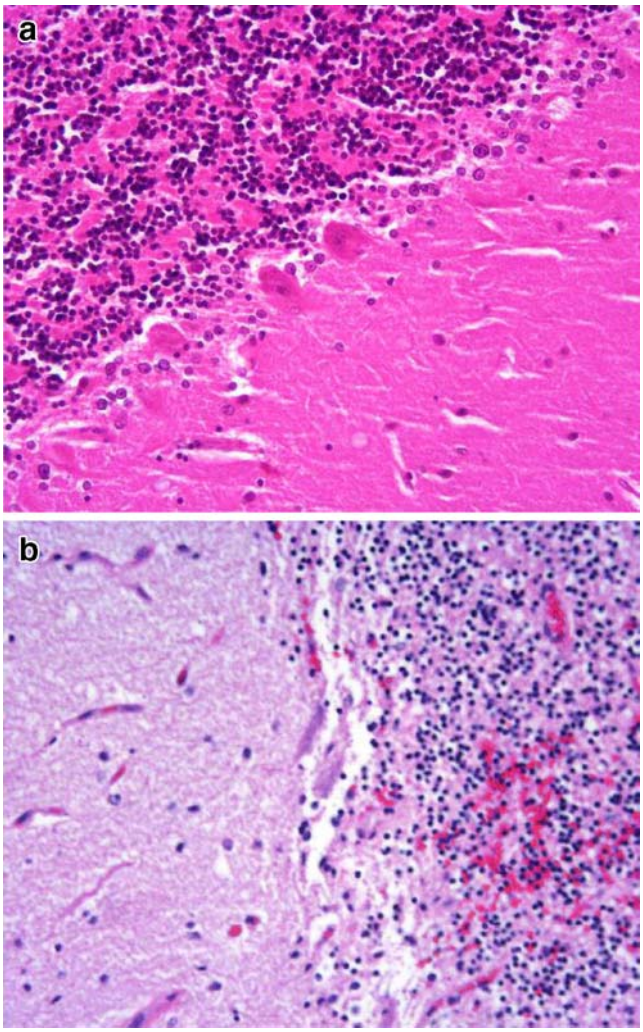

Fig. 1 **a** Fragment of normal cerebellum. **b** Severely sclerotic fragment of cerebellum with complete Purkinje cell loss

Discussion

Our results validate the findings of Koga et al. [5], who reported PCL and reactive gliosis in the cerebellar tonsils of patients with CMI. But while their conclusions were drawn from five individuals who had syringomyelia, our data drawn from a larger number of patients suggests that histological abnormalities of the cerebellar tonsils are common, but not obligatory in CMI patients.

Considering that in CMI the cerebellar tonsils descend into the cervical canal because of a shallow posterior fossa or as complication of the lumboperitoneal shunt, it is intuitive to presume that the changes that we observed are not the result of a diffuse anomaly that involves the whole cerebellar cortex, but that they are secondary to specific conditions that result from having a portion of CNS tissue trapped within a narrow canal.

The most frequent histological findings in our series were PCL and gliosis. Both conditions are linked to neuronal injury. Gliosis is widely recognized to be one of the earliest and most noticeable cellular responses after a wide variety of insults to the CNS [11]. It can be safely stated that there is hardly any pathology in the brain without an involvement of glial cells.

Similarly, PCL is found in a myriad of pathologies of the CNS that range from degenerative disorders to metabolic derangements and cerebral ischemia. With this in mind, the only two conditions that seem reasonable to forward as a hypothesis for histological changes seen in the cerebellar tonsils of CMI patients are ischemia and trauma.

While it has been demonstrated that the Purkinje cells are vulnerable to global cerebral ischemia, the patients in our series had neither a medical history nor clinical manifestations of global cerebral ischemia. If we assume that ischemia was a factor in PCL observed in our patient population, it has to be a focal phenomenon that probably resulted from chronic narrowing of arterial afferents to the neural tissue entrapped in the cervical canal. Several papers propose an association between ischemia and PCL. Welsh et al. [13] suggested that the reason Purkinje cells die so easily after global brain ischemia relates to the deficiency of aldolase C and EAAT4 that allow Purkinje cells to survive pathologically intense synaptic input from the inferior olive after restoration of blood flow. Their data imply that the two properties of Purkinje cells that make them susceptible to ischemic death are their reduced capability to sequester glutamate and a reduced ability to generate energy during anoxia. Martin et al. [7] attributed apoptosis and necrosis in the cerebellum after ischemia to anomalies in the glutamate receptor signaling pathways.

A more plausible explanation for the neural tissue damage is that the cerebellar tonsils are subjected to the constant strain of the pulsating passage of CSF in a constrained space. The cerebellum is susceptible in head injury. Fukuda et al. [2] and Mautes et al. [8] have documented PCL in experimental animals subjected to blunt brain trauma. PCL may be a consequence of alteration in the local microenvironment resulting from breakdown of the blood–brain barrier, subarachnoid hemorrhage, excitotoxicity, and/or neurotoxic molecules generated by reactive microglia.

Our hypothesis of local trauma being directly responsible for PCL is connected with the findings of Allen and Chase [1], who demonstrated that direct trauma injury to the cerebellar cortex causes gliosis and PCL but only after significant trauma.

Excitotoxicity is the common denominator triggering both ischemic and traumatic events. It is defined as " acute neuronal degeneration by excessive stimulation of postsynaptic EAA ionotropic receptors." According to Sarna and Hawkes [12], it is the unique design of the climbing fiber–Purkinje cell synapse that renders the latter vulnerable to excitotoxicity.

The cerebellar tonsils are the ventral paramedian structure of the cerebellar cortex. They receive pontocerebellar and spinocerebellar afferents. The patients do not have permanent damage that can be attributed to the preoperative or postoperative loss of the cortico-subcortical structures of the tonsils.

In the great majority of the cases, oculomotor and vestibular symptoms noted before surgery recede after surgery, thus suggesting that the symptoms resulted from the compression of the underlying medullar and pontine nuclei and not from altered cerebellar tissue.

Interestingly, five patients had normal findings. The tonsils were descended in all of them, and we failed to find a clinical common denominator between these children. Four of them were girls and two had syringomyelia.

It is not the intention of our report to advocate for cerebellar tonsillectomy as it is to share our findings with our colleagues.

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