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Rev Chil Pediatr. 2020;91(4):591-596
DOI: 10.32641/rchped.v91i4.1233

CLINICAL CASE

Dural ectasia and intracranial hypotension in Marfan syndrome

Ectasia dural e hipotensión endocraneal en síndrome de Marfán

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Received: May 23, 2019; Approved: February 01, 2020

What do we know about the subject matter of this study?

Dural ectasia is a common, though little known, characteristic in Marfan syndrome and other connective tissue disorders, which may be associated with intracranial hypotension syndrome.

What does this study contribute to what is already known?

This study presents a case of disabling headache secondary to intracranial hypotension syndrome to warn of this complication in children carriers of connective tissue diseases, especially with Marfan syndrome.

Abstract

Introduction: Marfan syndrome is an autosomal dominant, multi-systemic connective tissue disorder of different presentations. Dural ectasia is a common, but little known complication that can be associated with intracranial hypotension syndrome (IHS). **Objective:** To present a case of severe headache secondary to IHS in order to warn about this rare complication, which must be considered in children carriers of connective tissue diseases, especially Marfan syndrome. **Clinical Case:** 13-year-old female carrier of Marfan syndrome, clinically diagnosed according to the 2010 Ghent criteria, who consulted due to a 6-months history of severe orthostatic headache. Head magnetic resonance imaging (MRI) showed multiple signs of intracranial hypotension, while whole-spine MRI showed dural ectasia that caused the thecal sac dilation and subsequent remodeling of vertebral bodies, especially the sacral ones. Treatment with an autologous epidural blood patch was administered with good clinical response. **Conclusions:** Dural ectasia, frequent in Marfan syndrome, is a predisposing cause of cerebrospinal fluid (CSF) leakage, which could cause orthostatic headache secondary to IHS.

Keywords:
Marfan;
dural ectasia;
intracranial hypotension syndrome;
orthostatic headache

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How to cite this article: Rev Chil Pediatr. 2020;91(4):591-596. DOI: 10.32641/rchped.v91i4.1233

Introduction

Marfan syndrome is an autosomal dominant multi-system connective tissue disorder of variable expression, however, 25-30% of cases are sporadic mutations[1,2]. It has an estimated incidence of 2-3 per 10,000 live births, with no trend by sex or ethnic group[1]. Within the alterations associated with this syndrome, there have been identified mutations in the fibrillin-1 gene (FBN-1) and the transforming growth factor β (TGFβ) signaling pathway[2].

Marfan syndrome can affect several systems, including the cardiovascular, musculoskeletal, central nervous, pulmonary, ocular, and skin systems. The 2010 revised Ghent criteria are used for the diagnosis, where three main diagnostic elements are evaluated: aortic root dilation (Z score ≥ 2), ectopia lentis, and genetic study (FBN-1). The other major and minor criteria previously defined in the 1996 version of Ghent have today a lower value; they are grouped as systemic signs and are evaluated with a value scale (systemic score) that must be equal to or higher than 7 points to be significant[3,4].

Dural ectasia is defined as dilation of the dural sac and/or the nerve root sheaths, which was considered a major criterion in the diagnosis of Marfan syndrome (Ghent 1996), due to its low frequency in the general population and association with some specific disorders, such as Marfan syndrome, Ehlers-Danlos syndrome, neurofibromatosis, among others. It occurs in 63-95% of adult patients with Marfan syndrome and over 40% of children with this syndrome[5].

In most cases, dural sac widening occurs in the lumbosacral region. It has been suggested that higher continuous pulsatile pressure of the CSF in the lumbosacral area with the patient standing, would progressively affect a weakened and congenitally defective dural wall and spinal canal[l6]. This condition of secondary dilation and thinning of the thecal sac and/or nerve root sheaths predisposes to CSF leak through small fistulas in the thecal sac wall. CSF leak is the only proven cause, either iatrogenic such as lumbar puncture or spontaneous, for the occurrence of intracranial hypotension syndrome (IHS) and secondary neurological symptoms[6]. Dural ectasia and IHS are little known complications of Marfan Syndrome.

Objective

To present a case of disabling headache secondary to IHS to warn of this uncommon complication which should be considered in children carriers of connective tissue diseases, especially with Marfan syndrome.

Clinical Case

13-years-old female adolescent who consulted due to 6-month history of progressive headache. The headache suddenly occurs when standing up or sitting down, with a 10/10 intensity and it stops within 2 minutes of lying down. This condition severely limited her daily life activities and forced her to stay in bed. Among her family history, it is worth mentioning that her father died at the age of 50 due to cardiovascular pathology.

In the post-menarche stage (12 years), she presented a persistent increase in pubertal height, rapidly reaching 1.83 mt height and reported joint pain.

Physical examination showed skin with abundant stretch marks in scapula, thoracic, and breast regions, high-arched palate, crowded teeth, mild symmetrical pectus excavatum, ejection murmur in aortic area, and scoliosis. When examining the limbs, we observed arachnodactyly, long and thin arms, joint hypermobility, bilateral wrist and thumb sign, extension limitation in both elbows achieving 165 degrees angle, and bilateral flat foot.

In the cardiovascular evaluation, the electrocardiogram was normal and in echocardiography, we detected minor mitral regurgitation and mild aortic root dilation, with a 3.5 Z score.

Full anteroposterior and lateral spine imaging showed rightward convexity in the coronal plane with 22 degrees of Cobb angle and thoracolumbar hyperkyphosis of 52 degrees.

The characteristics described in the physical examination, in addition to the findings in complementary examinations, raised the diagnosis of Marfan Syndrome. According to the 2010 Ghent criteria, the girl presents aortic root dilation (Z score ≥ 2) added to 7 or more systemic points (systemic score) for the diagnosis of the syndrome.

Brain and spine MRI and CT scans of the lumbar area were performed. Brain MRI with contrast performed for studying her headache showed signs of intracranial hypotension (figures 1 and 2) characterized by caudal angulation of the posterior third of the corpus callosum, cerebellar tonsillar ectopia, caudal displacement of the brainstem, epidural venous plexus engorgement, and pituitary gland and supratentorial dural enhancement. In order to identify the origin of intracranial hypotension, a full-spine MRI was performed which showed dural ectasia (Figure 3) that causes thecal sac dilation and subsequent remodeling of the vertebral bodies, which was more significant in the sacrum region. The presence of dural ectasia predisposes to CSF leak and IHS, which is not iatrogenic and would be the cause of the girl's disabling orthostatic headache.

The patient was treated with epidural blood patch of autologous blood, presenting little response initially and, in a second attempt, a good therapeutic response was achieved.

Discussion

Dural ectasia in Marfan syndrome is generally asymptomatic, however, it can present neurological symptoms, such as low back pain, headache, pain and paresthesia in lower limbs, genital and rectal pain which are exacerbated when standing up[7]. It may occur along with spondylolisthesis, scoliosis, and anterior sacral meningocele, the latter appearing as a pelvic mass.

Dural ectasia or dural sac dilatation, with subsequent spinal canal enlargement in any segment along the spine, usually occurs in the lower lumbar and sacral regions, with cortical thinning of the pedicles and the lamina of the vertebrae, neural foraminal widening, or the presence of an anterior meningocele[1,8].

In plain x-ray, we observe interpedicular distance widened on anteroposterior projection and posterior vertebral scalloping on lateral projection, with high specificity, but low sensitivity[9].

CT scan and MRI have proven to be the imaging procedures of choice for diagnosis. They offer a multiple-planes assessment and allow an adequate evaluation of the extent of the dural sac and/or nerve root sheath dilation, the presence of meningocele or associated arachnoid cysts, bone erosions in the posterior aspects of the vertebral bodies, and neural foraminal widening, especially in the lumbar-sacral region[1,8].

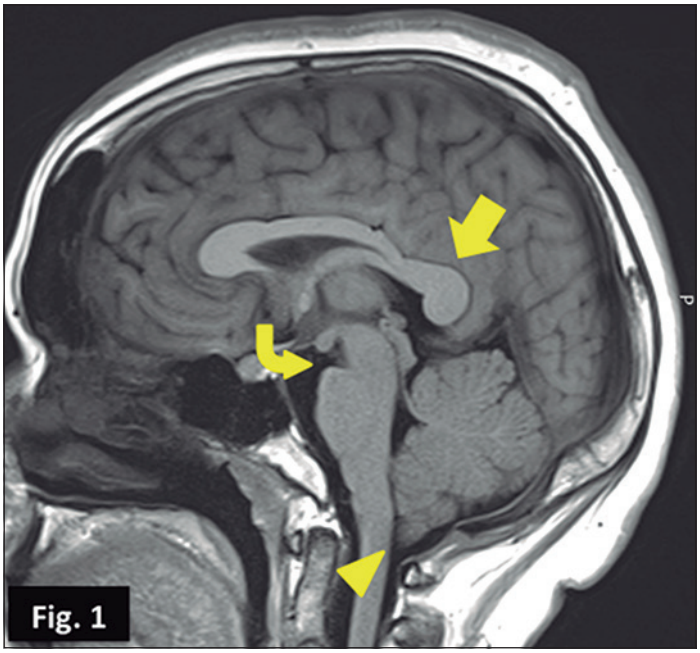

Figure 1. Magnetic Resonance Imaging (MRI) of the brain in sagittal T1 sequence without contrast. Signs of endocranial hypotension characterized by caudal angulation of the posterior third of the corpus callosum (arrow) and descent of the cerebellar tonsils (arrowhead) are recognized. Subtle caudal caudal displacement of the brainstem (curved arrow) is also observed.

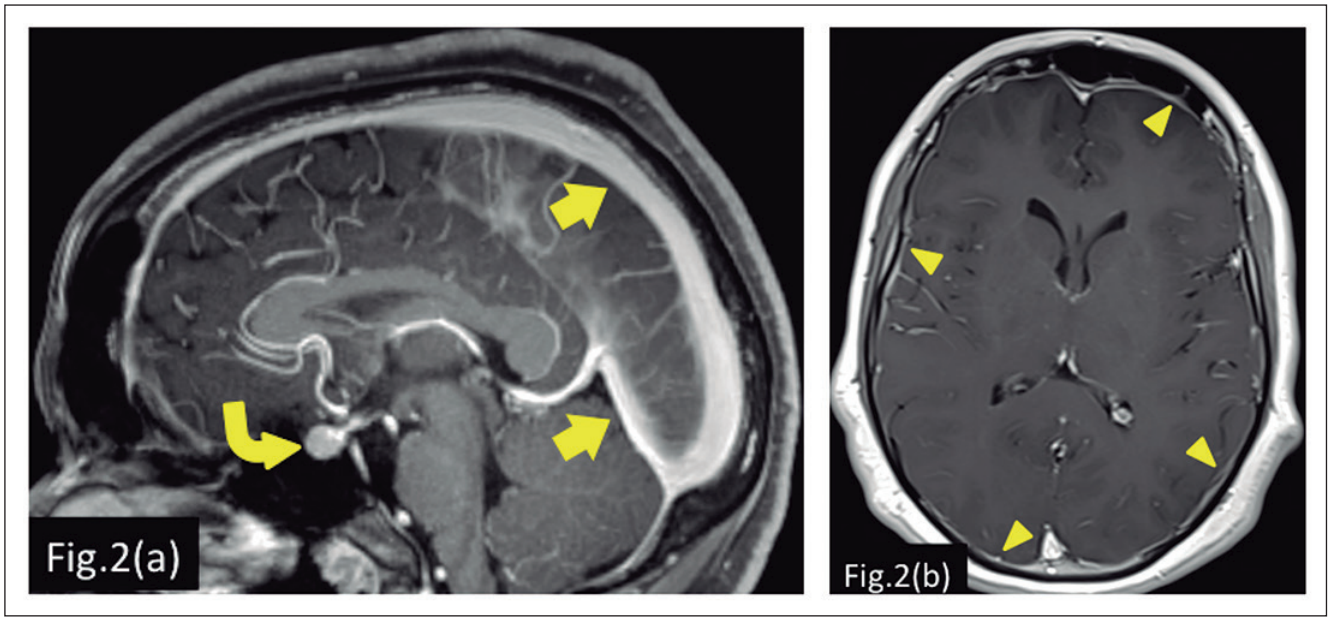

Figure 2. The use of intravenous contrast is essential for the characterization of other signs of endocranial hypotension visible on brain MRI. **A:** Brain MRI in sagittal T1 sequence with contrast, evidence of ingurgitation of the upper sagittal and rectal dural venous sinuses (arrows). There is also enlargement of the pituitary gland (curved arrow). **B:** Brain MRI in axial T1 sequence with contrast, shows bilateral symmetrical supratentorial dural thickening and enhancement (arrowhead).

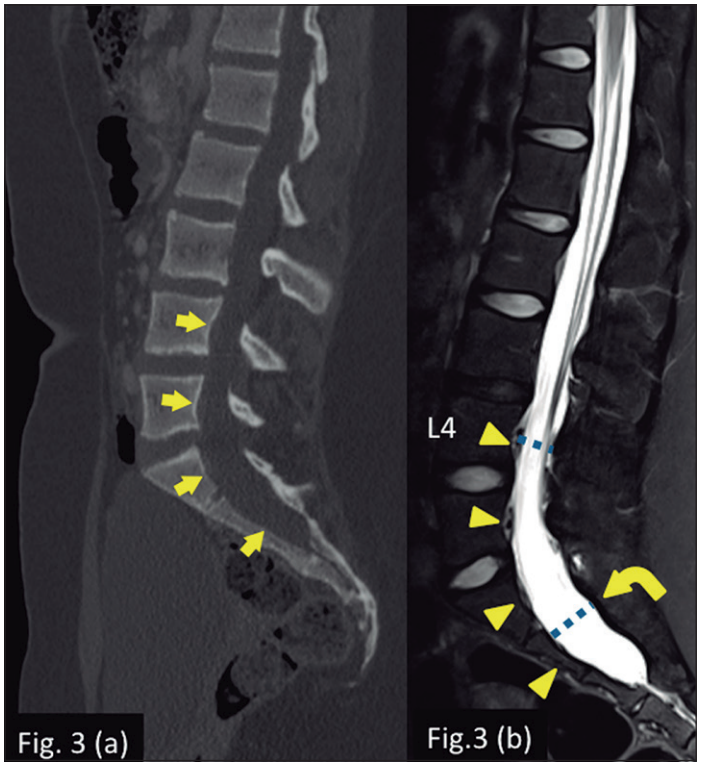

Figure 3. A. Lumbar spine computed tomography (CT) sagittal reformatting. Remodeling of the posterior wall of the vertebral bodies from L4 to S3 is observed (arrows). **B.** Magnetic Resonance Imaging (MRI) of the lumbar spine in sagittal T2, confirms the presence of a dilation of the tecal sac, which determines the posterior remodeling of the vertebral bodies (arrowheads). The widening is more significant at the level of the sacrum (curved arrow), where it is wider than at L4 (dotted lines), a major criterion of dural ectasia.

MRI has the advantage of allowing a comprehensive assessment of the neuraxis (spine/root and bone), identifying the cause, and evaluating differential diagnoses. Computed tomographic myelography is a study where contrast material is injected through a lumbar puncture to the subarachnoid space and a CT image acquisition is performed to identify the site of CSF leak. This procedure is highly sensitive and specific, however, it uses ionizing radiation and is invasive, so it is used for cases that require particular treatment[10]. Regardless of the method, it is not common to identify the leak site[11].

Ahn et al. described in MRI, that dural ectasia is occurring if there are one major or two minor criteria. The major criteria are dural sac width below S1 greater than L4 or above L4 and presence of an anterior sacral meningocele, and the minor criteria are posterior vertebral scalloping of the vertebral body S1 > 3.5 mm and diameter of nerve root sheath > 6.5 mm at L5[12].

Oosterhof et al. also describe quantitative criteria for dural ectasia in MRI. They calculate the diameter ratio of the dural sac divided by the width of the vertebral bodies in the mid-sagittal plane at L1 to S1 or DSR (dural sac ratio), which must be greater than 0.64 at L1, 0.55 at L2, 0.47 at L3, 0.48 at L4, 0.48 at L5, and 0.57 at S1 in adult patients[13-15]. In children, there are no established criteria, however, when applying the criteria described to our patient, they were positive for the diagnosis of dural ectasia.

Differential diagnoses of dural ectasia include congenital arachnoid cysts and intradural tumors that widen the spinal canal. When dural ectasia extends to the pelvis as an anterior sacral meningocele, it can look like a pelvic mass[16].

One of the known complications of dural ectasia is IHS. This syndrome can be caused by multiple etiologies, however, all of them have a common physiopathology, the CSF leak somewhere in the central nervous system (CNS), which is most frequent at the dorsal-lumbar level. The CNS is a closed system where intracranial pressure (ICP) is higher than atmospheric pressure and can vary with a disease or in a physiological way such as changes in position (supine versus standing) as well as with maneuvers such as the Valsalva one. This explains postural or orthostatic headache, where there is an increase in intensity when sitting and a decrease when lying down[10].

The constant and abundant CSF leak generates a decrease in ICP and eventual suction and descent of the brain, as it would be in our case. The loss of ICP is initially compensated through hemodynamic mechanisms that can be identified through imaging studies and thus pose a prospective diagnosis of this syndrome. The alterations become progressively evident as the compensation mechanisms are overcome. Initially, venous engorgement and pituitary gland enlargement are observed, as well as dural thickening and enhancement.

As the loss of CSF increases, the corpus callosum and brain stem begin to progressively descend. This appears as cranial/caudal direction of the posterior third of the corpus callosum, descent of the cerebellar tonsils, and caudal displacement of the brainstem. Another mechanism is the formation of symmetrical bilateral supratentorial subdural collections, with or without associated bleeding, which can reach significant volumes, and even lead to incorrect attribution of the symptomatology. Eventually, the descent of the brain stem can lead to compression and herniation through the foramen magnum, with high morbidity and mortality[17].

In our patient, there was no known cause of CSF leak (e.g. bypass valve) thus a complete spinal assessment was performed to try to identify it, determining the presence of dural ectasia. In general, the most frequent causes are spontaneous ruptures of perineural cysts or spinal meningeal diverticula.

In both children and adults, they will present clini-

cally as orthostatic headache, however, unlike adults, up to 54% of children with IHS may have associated connective tissue disease[18].

It is relevant to recognize imaging findings to guide the study and to perform a systemic evaluation when there is no history. In addition, it is important to bear in mind that a patient with Marfan syndrome or another connective tissue disease may present with orthostatic headache due to intracranial hypotension, and should, therefore, be studied since she/he is at risk of morbidity and mortality[19].

Management will depend on the location and size of the meningeal gap. In our case, the blood patch was used successfully which is the most widely used treatment. Fibrin patches are also commonly used, however, these are directed to the most suspicious site of the leak (e.g., larger diverticulum), thus requiring prior imaging evaluation. Surgery is generally reserved for refractory cases[10].

Conclusion

Dural ectasia is a cause of intracranial hypotension that can explain orthostatic headache in patients with Marfan syndrome, therefore, it is important to know this complication with eventual morbidity-mortality, study techniques, and radiological findings of this pathology.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

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