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Intracranial hypertension in 2 children with Marfan syndrome

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Introduction

Marfan syndrome (OMIM 154700) is a connective tissue disorder with multisystemic involvement and autosomal dominant inheritance due to mutations in the fibrillin-1 gene (FBN1).

Here we report two unrelated children with Marfan syndrome and recurrent intracranial hypertension. To our knowledge, intracranial hypertension (IH) has never been associated with Marfan syndrome.

Case report

The first case is an 11-year-old boy with Marfan syndrome who presented with headache, nausea and vomiting on several occasions. The intracranial pressure at these events was measured to be above 20 cm H₂O. His symptoms disappeared after drainage of at least 15 cc of cerebrospinal fluid (CSF). Extensive investigations revealed only mild iron deficiency anemia. Treatment of the anemia did not prevent a new episode of high intracranial pressure. Magnetic resonance imaging (MRI) of the brain showed bilateral choroid plexus cysts, slightly dilated ventricles, and a small arachnoid cyst of 1.5 cm in the cisterna magna (Figure 1A). The spinal cord MRI showed sacral dural ectasia with radicular cysts and an anterior sacral meningocele (Figure 1B and 1C). The diagnosis Marfan syndrome was made in the first year of life because of lens subluxation and a positive family history. At age 11 he has mild skeletal manifestations of Marfan (pes planus) and a mildly dilated aortic root. His length is on the 84th centile, his weight on the 80th centile and his head circumference on the 50th centile. He has had several ophthalmological operations for lens luxations and strabismus. He fulfills the international criteria for Marfan syndrome. A homozygous missense mutation in exon 60 of the fibrillin-1 gene was found, leading to the amino acid substitution p.Asp2485Val. Both parents carry one copy of the mutation and exhibit very minor signs of Marfan syndrome. His affected sister also has a homozygous mutation. She has the classical manifestations of Marfan syndrome but does not have signs of high intracranial pressure.

The second case was a 7.5 year old girl who was evaluated for complaints of headache, vomiting, diplopia and a tonic clonic epileptic seizure. Apart from papil edema there were no neurological signs. After excluding intracranial mass lesions or vascular lesions, a lumbar puncture was done revealing a CSF pressure of 50 cm H₂O. Repeated lumbar punctures were necessary to alleviate her symptoms. Medical treatment was started with acetazolamide that relieved her headache and controlled the CSF pressure (8 cm H₂O). After discontinuing the medication the symptoms returned promptly. A ventricular
peritoneal drainage operation was performed with excellent result. Physical examination showed a length far above the 99th centile, arm span on the 75th centile, weight on the 80th centile and head circumference on the 90th centile. Her joints were hypermobile. Because of the high intracranial pressure and her body habitus, extensive analysis was performed for connective tissue disorders and diseases causing high intracranial pressure. Endocrinological tests, X-rays of the vertebral column, an extensive metabolic screen, including vitamine disorders, showed no abnormalities. MRI of the brain and spinal cord showed narrowing of the left transverse sinus and mild ectasia of the dural sac. At echocardiographic examination mild prolapse of the mitral- and tricuspid valves and aortic root dilation were detected. The clinical diagnosis Marfan syndrome was made according to the international criteria. The diagnosis was confirmed by a de novo missense mutation in the fibrillin-1 gene (7741T>A) leading to the amino acid substitution Cys2581Ser.

Figure 1. Magnetic resonance T2-weighted turbo spin-echo images of the brain and spine of case 1. (A) Transverse brain image demonstrating bilateral plexus choroideus cysts (arrows). (B) Transverse image showing the anterior sacral meningocele. (C) Sagittal image of the lumbosacral spine showing dural ectasia (arrow) and scalloping of the posterior lumbar vertebral bodies (arrowheads).
Discussion

Although severe headache has been reported in Marfan syndrome due to intracranial hypotension caused by CSF leakage from dural ectasia, this is the first report of intracranial hypertension in Marfan patients. The choroid plexus cysts and the arachnoid cyst present in case 1 might have contributed to the raised intracranial pressure by impairment of CSF flow. Cerebrovenous sinus abnormalities, as present in case 2, are frequently found in idiopathic intracranial hypertension but whether such findings result from or cause the raised pressure is still unknown. The intracranial lesions as described in case 1 and 2 have not been previously associated with Marfan syndrome.

Given the low incidence of both intracranial hypertension in children and Marfan syndrome, the concurrence of intracranial hypertension with Marfan syndrome in two young patients is unlikely to be coincidental. Marfan syndrome, and possibly other connective tissue disorders, may confer a predisposition to developing intracranial hypertension. Therefore, patients with Marfan syndrome and unexplained symptoms of headache and vomiting should be promptly investigated for possible intracranial hypertension, and conversely, in young patients with unexplained intracranial hypertension possible signs of Marfan syndrome should be noted and, if so, further investigations instigated.

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References


