Spontaneous intracranial hypotension from a CSF leak in a patient with Marfan’s syndrome

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Abstract
A patient with Marfan’s syndrome had spontaneous intracranial hypotension secondary to a proved CSF leak. It is postulated that the leak was caused by minor, unrecognised trauma rupturing spinal arachnoid diverticula. The diverticula were probably pre-existing abnormalities complicating the Marfan’s syndrome. It is concluded that patients with spinal meningeal defects may be at increased risk of developing CSF leaks, possibly secondary to unrecognised trauma.

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Spontaneous intracranial hypotension is a very rare cause of headache. We present a recurrent case of this syndrome secondary to an established CSF leak from the spinal subarachnoid space occurring in a patient with Marfan’s syndrome. We suggest a possible pathophysiological mechanism and describe the therapeutic options.

Case report
This woman first presented in 1992 at the age of 19 years with a six week history of worsening headache for which no clear precipitant could be identified. The pain was concentrated over the right side of the head and throbbing in nature. There was a dramatic postural component such that the pain was virtually eliminated by lying flat, only to return within a minute or two of sitting up. Associated with the headache were nausea and vomiting but no visual symptoms. Although otherwise well, the headaches were severe enough to warrant emergency admission to hospital.

She was known to have Marfan’s syndrome; previous cardiological assessment had disclosed mitral valve prolapse and borderline aortic root dilatation. Her mother also had Marfan’s syndrome and had undergone aortic valve replacement. There was no other relevant history; in particular she had never previously had headaches. She was not taking any medication.

Examination showed a typical marfanoid habitus with arachnodactyly, tall stature, pectus excavatum, and joint hyperextensibility; auscultation disclosed multiple midystolic clicks consistent with mitral valve prolapse. There were no neurological signs. Sitting or standing resulted in a rapid resurgence of her symptoms with accompanying vomiting and pronounced distress; all symptoms abated within minutes of lying flat.

Routine haematological and biochemical tests were normal as was unenhanced cranial CT. A lumbar puncture was attempted; no CSF could be obtained for analysis but it was noted that clear fluid was visible in the hub of the needle on expiration. A repeat CT showed air in the basal cisterns confirming that the opening pressure had indeed been less than atmospheric. While further investigations were being considered, the headaches resolved spontaneously and she was discharged from hospital.

Identical symptoms recurred two years later. By the time of admission she was confined to bed and requiring regular opiate analgesia to combat the headaches; on a visual analogue score the patient judged these headaches as 9 out of 10 (10 being the most severe). As before, neurological examination was normal.

A diagnosis of recurrent intracranial hypotension was made and investigations directed to identify a CSF leak. Unenhanced CT was normal apart from slit-like ventricles. Radioisotope cisternography showed an abnormal accumulation of isotope on the left at the level of T1–3 with multiple smaller bilateral projections at most levels of the thoracic spine (fig 1). In addition there was early renal excretion of radioisotope. Computed tomographic myelography disclosed contrast extruding from the left neural foramen at T1 (fig 2) with a small amount of contrast passing medially to the pleura. In the lumbar region there were multiple large arachnoid diverticula around the lumbrosacral nerve roots (fig 3) with some erosion of the sacrum. Analysis of CSF was normal.

Because of her debilitating symptoms, a lumbar epidural catheter was inserted and a saline infusion started; within two hours she was able to sit up and walk for the first time in several weeks with no symptoms. After five
leak, with 30 ml autologous blood, resulted in considerable improvement of her symptoms (analogue score 1–2 out of 10) and she was able to mobilise freely for the first time in several weeks. She remained well for six weeks before her symptoms returned, although with less intensity. A repeat thoracic epidural blood patch was performed; a subsequent radioisotope cisternogram, by contrast with the first examination, showed no residual leak (fig 1). At her last review, three months after the second epidural patch, her headache score was 3–4 out of 10 and she was continuing to take regular analgesia but was able to work.

Discussion
Spontaneous intracranial hypotension was first described by Schaltenbrand in 1938. He proposed three possible causal mechanisms; increased absorption, decreased production, or leakage of CSF. There is little evidence to support the first two mechanisms, chiefly because no techniques to directly measure CSF production or absorption are currently available. Labadie et al described a patient with spontaneous intracranial hypotension who on cisternography showed rapid disappearance of radioactive tracer from the subarachnoid space and early renal excretion; they concluded that this would be consistent with either hyperabsorption of CSF or an unidentified leak. There are other reports claiming support for the hyperabsorption theory. The meningeal enhancement seen on MRI in spontaneous intracranial hypotension has been interpreted as compatible with either decreased CSF production or increased absorption; others suggest that the enhancement is simply a result of dilatation of the meningeal vasculature secondary to a reduced CSF volume. In their comprehensive review of spontaneous intracranial hypotension, Rando and Fishman dismissed the hyperabsorption hypothesis, arguing that no appreciable absorption occurs at low CSF pressures and concluded that CSF leakage from the neuroaxis is the most likely mechanism. As in our case, radioisotope cisternography may identify such a leak. Our patient undoubtedly had spontaneous intracranial hypertension according to suggested criteria and subsequent investigations combined with the response to treatment provide compelling evidence that the cause was CSF leakage from an arachnoid diverticulum, a defect associated with Marfan’s syndrome.

Marfan’s syndrome is caused by mutations of the fibrillin gene on the long arm of chromosome 15 (15q). The primary neurological complications are dural ectasia, meningoceles, learning disability, and hyperactivity. Dural ectasia is the most common, occurring in 63% in one CT study, although there was no association with the severity of the Marfan’s syndrome. Meningoceles, usually of the lumbosacrum, and arachnoid diverticula or cysts are also well recognised; it has been suggested that these defects develop secondary to the normal, continuous, pulsatile
Figure 3  Lumbar myelogram showing multiple large arachnoid diverticula.

CSF pressure together with unrecognised trauma acting on a structurally weakened dura,\(^\text{12,10}\) Arachnoid cysts occurring in the normal population may also be due to the effects of previous minor trauma.\(^\text{22}\) Intracranial hypotension after minor trauma to the head\(^\text{8}\) or spine\(^\text{23,24}\) in patients without Marfan's syndrome has been reported; in some cases an obvious dural leak has been identified,\(^\text{22}\) whereas in others a leak was assumed although unidentified.\(^\text{24}\)

Postural headaches associated with Marfan's syndrome and dural abnormalities have been described before. Raftopoulos et al\(^\text{13}\) reported a case presenting with back and thigh pain; in addition there was a history of intermittent postural headaches which had settled spontaneously. Investigation disclosed a large sacral meningocele and they postulated that the headache was the initial symptom of this lesion, the meningocele acting as a reservoir for CSF when the patient stood up, resulting in a low intracranial CSF pressure. Stern\(^\text{26}\) described a patient who presented with sudden onset of low back pain radiating into both legs associated with a postural headache. Myelography showed multiple diverticula exiting the sacral foramina with a grossly ectatic lumbosacral theca; insertion of a lumboperitoneal shunt resolved her back and leg pain but unsurprisingly not the headache, which took several months to settle spontaneously. Cisternography was not done in either of these two patients.

In many of the reported cases of spontaneous intracranial hypotension, the symptoms have resolved spontaneously with no specific treatment required. Our patient’s recurrent headache, however, led to her being confined to bed in hospital for several weeks, necessitating some kind of intervention. Both epidural saline infusion and autologous blood patching are described as efficacious in the management of low pressure headaches.\(^\text{26,27}\) We elected to try an epidural infusion first for both diagnostic and therapeutic reasons. Although we were unable to complete the planned infusion of 48 hours, the brief, immediate response was impressive. We then performed blood patching, initially at the lumbar level because of technical unease at injecting at the thoracic level; when this failed, the thoracic approach was used with success and no complications. This confirms the suggestion of Szeinfeld et al that although injected blood may spread cranially over several segments, the best results follow injection within one interspace of the dural leak.\(^\text{22}\) Although there is no reason to suspect that this form of treatment will protect our patient from further dural tears at other sites in the future, it has enabled her to return to a near normal life at present.

Conclusions
We have presented a case of spontaneous intracranial hypotension secondary to a proved CSF leak occurring in a patient with Marfan’s syndrome; to our knowledge this is the first published case. We postulate that the leak was caused by minor, unrecognised trauma rupturing one or more spinal arachnoid diverticula. These diverticula were probably pre-existing abnormalities complicating the Marfan’s syndrome. We conclude that patients with spinal meningeal defects may be at increased risk of developing such leaks, possibly secondary to unrecognised trauma. We agree with others that radioisotope cisternography is the investigation of choice to identify the site of any CSF leak and that site specific epidural blood patching is the best treatment for severe symptoms.

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