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Accuracy of brain imaging in the diagnosis of idiopathic intracranial hypertension

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AIM: To investigate the accuracy of individual and combinations of signs on brain magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) in the diagnosis of idiopathic intracranial hypertension (IIH).

MATERIALS AND METHODS: This study was approved by the institutional research ethics board without informed consent. Forty-three patients and 43 control subjects were retrospectively identified. Each patient and control had undergone brain MRI and MRV. Images were anonymized and reviewed by three neuroradiologists, blinded to clinical data, for the presence or absence of findings associated with IIH. The severity of stenosis in each transverse sinus was graded and summed to generate a combined stenosis score (CSS). The sensitivity, specificity, and likelihood ratios (LR) were calculated for individual and combinations of signs.

RESULTS: Partially empty sella (specificity 95.3%, $p < 0.0001$), flattening of the posterior globes (specificity 100%, $p < 0.0001$), and CSS <4 (specificity 100%, $p < 0.0001$) were highly specific for IIH. The presence of one sign, or any combination, significantly increased the odds of a diagnosis of IIH (LR+ 18.5 to 46, $p < 0.0001$). Their absence, however, did not rule out IIH.

CONCLUSIONS: Brain MRI with venography significantly increased the diagnostic certainty for IIH if there was no evidence of a mass, hydrocephalus, or sinus thrombosis and one of the following signs was present: flattening of the posterior globes, partially empty sella, CSS <4. However, absence of these signs did not exclude a diagnosis of IIH.

Introduction

Idiopathic intracranial hypertension (IIH), also known as benign intracranial hypertension or pseudotumour cerebri, is characterized by increased cerebrospinal fluid (CSF) pressure in the absence of an identifiable structural cause.[1–3] IIH typically occurs in young and overweight female patients who develop symptoms and signs of raised intracranial pressure, including headache, visual disturbances, pulsatile tinnitus, and papilloedema.[1–3] Diagnosis is typically confirmed by a lumbar puncture, which demonstrates raised CSF pressure with normal composition.[1–3] Neuro-imaging has been traditionally used to exclude other causes of increased intracranial pressure such as mass lesions, hydrocephalus, or venous sinus thrombosis.[1–3]

Certain signs on cross-sectional imaging have been reported to be associated with IIH,[4–17] including flattening of the posterior aspect of the globes, protrusion of the

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intraocular portion of the optic nerve, vertical tortuosity of the optic nerve, distension of the optic nerve sheaths, enhancement of the optic nerve head, partial empty sella turcica, slit-like ventricles, tight subarachnoid spaces. However, these cross-sectional imaging findings are non-specific and can be seen in association with other conditions or causes of raised intracranial pressure.[18–20] Venography is also necessary in the workup of patients with IIH in order to rule out venous sinus thrombosis, which can mimic IIH in clinical presentation.[21] A high proportion of patients with IIH have been found to have bilateral severe transverse sinus stenosis using magnetic resonance venography (MRV).[22,23] Thus, the combination of findings from cross-sectional imaging, in addition to the presence of non-thrombotic transverse sinus stenosis on MRV, would be expected to be highly specific for IIH. However, few studies have examined the diagnostic utility of these individual magnetic resonance imaging (MRI) signs for IIH[4,6,11,22,23] or combinations thereof,[4] and only one group has examined their inter-rater reliability.[4,22] No published study has specifically evaluated the utility of combining the cross-sectional imaging signs with findings on MRV in the diagnosis of IIH.

The objectives of the current study were threefold: (a) to assess the sensitivity, specificity, and inter-observer reliability of individual MRI imaging (cross-sectional and venographic) signs associated with IIH; (b) to compare the sensitivity of time of flight (TOF) and contrast-enhanced (CE) MRV techniques in the detection of severe transverse sinus stenosis; (c) to determine whether the combination of cross-sectional MRI and MRV findings increases the diagnostic certainty for IIH.

Materials and methods

This study was approved by The Ottawa Hospital Research Institute Research Ethics Board without informed consent.

Patients

Forty-three patients were identified at The Ottawa Hospital between 2003–2009 based on the availability of a brain MRI and MRV. Patients were excluded from further analysis if they had surgical treatments such as optic nerve sheath fenestration, ventriculoperitoneal, or lumboperitoneal shunt, transverse sinus stenting or subtemporal decompression, prior to the brain MRI and MRV. Patients in the IIH group were diagnosed and treated by an experienced neuro-ophthalmologist and a neurologist. All patients had symptoms or signs of raised intracranial pressure including headache (38/43, 88%), papilloedema (42/43, 98%), and transient visual obscurations (19/43, 44%). Neurological examination was otherwise normal with the exception of unilateral cranial nerve VI palsy in one patient. Neuro-imaging ruled out a mass lesion, hydrocephalus, or sinus thrombosis in all patients. Mean and median CSF pressure was 34 cm water (SD 9.8; min. 22, max. 55) as determined by lumbar puncture. CSF pressures were unavailable in three patients who refused lumbar puncture, and felt to be inaccurate in three patients due to multiple dural punctures or significant leakage and loss of cerebrospinal fluid prior to measurement of pressure (opening pressure 14, 14, and 21 cm water). These six patients otherwise fulfilled modified Dandy criteria for IIH[24,25] and had a clinical course consistent with IIH and, therefore, were included in subsequent analyses.

Controls

All MRV studies performed between 2008 and 2009 at The Ottawa Hospital were reviewed and a control group of 43 subjects was identified based on the availability of a brain MRI and MRV reported as normal by a neuroradiologist. Specifically, studies reported to have any evidence of acute or chronic ischaemic stroke, haemorrhage, demyelination, mass lesion, hydrocephalus, intracranial hypotension, or venous sinus thrombosis were excluded from further analysis. Patients diagnosed with IIH as determined by a review of the electronic medical records of all control patients, were also excluded from the control group. Patients were not excluded from the control group on the basis of the appearance of the globe, pituitary, or venous sinuses, unless sinus thrombosis was suspected. The clinical indications for the brain MRI and MRV in the control group were: severe or refractory headaches ($n = 17$; 40%), headaches during pregnancy ($n = 7$; 16%), headaches in a patient with a known thrombophilia [$n = 4$; 9%: systemic lupus erythematosus (SLE) $n = 2$, prior deep venous thrombosis $n = 2$], possible uni- or bilateral optic disc swelling ($n = 6$; 14%), eclampsia ($n = 3$; 7%), suspected intracranial hypotension ($n = 3$; 7%), hyperdense appearance of the venous sinuses on a computed tomography (CT) examination of the head in a patient with cancer ($n = 2$; 5%), and isolated pulsatile tinnitus ($n = 1$; 2%). Of the six patients with possible optic disc swelling, five were subsequently diagnosed with pseudopapilloedema and one with papillitis/optic neuritis. CSF pressures were not available for patients in the control group.

Imaging

Imaging was performed on 1.5 T (Siemens, Symphony-Tim MRC 37144 or Symphony MRC 14022, Siemens Medical Solutions, Malvern, PA, USA) or 3-T (Siemens, TrioTim MRC 35382, Siemens Medical Solutions, Malvern, PA, USA) MRI systems. On the 1.5 T system, three-dimensional (3D) contrast-enhanced (CE) MRV was performed using 6.6 ms repetition time (TR), 2.21 ms echo time (TE), 25° flip angle, and 0.75 mm section thickness, and 235 mm field of view. The two-dimensional (2D) time of flight (TOF) MRV was performed with 28 ms TR, 6.5 ms TE, 30° flip angle, 3 mm section thickness, and 225 mm field of view. On the 3 T system, 3D CE MRV was performed with 5.7 ms TR, 1.93 ms TE, 30° flip angle, 0.75 mm section thickness, and 240 mm field of view. The 2D TOF MRV was performed with 48.9 ms TR, 8.19 ms TE, 15° flip angle, 0.90 mm section thickness, and 200 mm field of view. To avoid in-plane loss