Imaging signs in idiopathic intracranial hypertension: Are these signs seen in secondary intracranial hypertension too?

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Abstract

Background: The purpose of this study was to evaluate the difference in the occurrence of the various "traditional" imaging signs of intracranial hypertension (IIH) on magnetic resonance imaging (MRI) in patients with idiopathic (IIH) and secondary intracranial hypertension. **Materials and Methods:** In a retrospective analysis, the MRI findings of 21 patients with IIH and 60 patients with secondary intracranial hypertension (41 with tumors; 19 with intracranial venous hypertension) were evaluated for the presence or absence of various "traditional" imaging signs of IIH (perioptic nerve sheath distention, vertical buckling of optic nerve, globe flattening, optic nerve head protrusion and empty sella) using the Fisher's exact test. Odds ratios were also calculated. Statistical Package for the Social Sciences version 17.0 was used for statistical analysis. Subgroup analysis of the IIH versus tumors and IIH versus venous hypertension were performed. **Results:** Optic nerve head protrusion and globe flattening were significantly associated with IIH. There was no statistically significant difference in the occurrence of rest of the findings. On subgroup analysis, globe flattening and optic nerve head protrusion occurred significantly more often in IIH than in tumors. However, there was no statistically significant difference in the occurrence of any of these findings in patients with IIH and venous hypertension. **Conclusions:** IIH is a diagnosis of exclusion. While secondary causes of raised intracranial pressure (ICP) have obvious clinical findings on MRI, some conditions like cerebral venous thrombosis may have subtle signs and differentiating between primary and secondary causes may be difficult. In the absence of any evident cause of raised ICP, presence of optic nerve head protrusion or globe flattening can suggest the diagnosis of IIH.

Key Words

Intracranial hypertension, magnetic resonance imaging, signs

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Introduction

Raised intracranial pressure (ICP) may be due to a known secondary cause like mass lesions, meningitis, venous sinus thrombosis or hydrocephalus, or it may be "idiopathic." Idiopathic intracranial hypertension (IIH) is a syndrome of elevated ICP without any identifiable brain pathology and with normal cerebrospinal fluid (CSF) composition.[1,2] The cause of this raised ICP is unknown and diagnosis requires the exclusion of other secondary causes of raised pressure like tumors, infective lesions and obstruction to CSF flow or venous outflow like venous sinus thrombosis or dural arterio-venous fistulas.[3]

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Both IIH and venous thrombosis may lead to attenuation of the venous sinuses due to raised ICP. The differentiation of these two conditions may be difficult even on venographic studies.[4] Recognition of a secondary cause of raised ICP like venous sinus thrombosis or the diagnosis of IIH has crucial therapeutic and prognostic implications.

Many imaging signs of IIH have been described in literature[5-7] including perioptic nerve sheath distention, vertical buckling of optic nerve, globe flattening, optic nerve head protrusion and an empty sella. The purpose of this study was to evaluate the difference in the occurrence of these various "traditional" imaging signs in patients with IIH and secondary intracranial hypertension.

Materials and Methods

Study design and patient selection

We performed a retrospective analysis of the magnetic resonance imaging (MRI) findings of imaging in a cohort of 81 patients with intracranial hypertension scanned over a period of 2 years (May 2008 to August 2010). Of these, 21

patients had confirmed IIH and 60 patients had secondary intracranial hypertension (41 with tumors; 19 with venous hypertension [17 with venous sinus thrombosis and 2 with dural arterio-venous fistulas]). The images were evaluated for the presence or absence of various "traditional" imaging signs of IIH. Consent was obtained from patients before performing the imaging. As this was a retrospective review, institutional review board approval was waived.

The clinical details of patients were obtained from the medical database. All the patients with IIH were diagnosed on the basis of elevated opening pressures (more than 250 mm of water) on lumbar puncture and fundoscopy. The patients with known secondary causes of intracranial hypertension (tumors and venous hypertension) were diagnosed to have elevated intracranial tension based on the presence of bilaterals papilledema on fundoscopic examination. Lumbar puncture with quantification of CSF opening pressures was not done in this subgroup due to the invasive nature of this test.

Imaging technique and image analysis

MRI was performed on a 1.5 T clinical magnetic resonance scanner (Seimens Magnatom Avanto, Erlangen, Germany) using a 12 channel transmit receive head coil. While all the sequences, including T2, Fluid attenuated inversion recovery sequence fluid attenuated inversion recovery sequence (FLAIR), and T1 weighted images were obtained in all the patients; T2 weighted images in sagittal and coronal orientation (5 mm) were studied for the presence or absence of perioptic nerve sheath distention, vertical buckling of optic nerve, globe flattening, optic nerve head protrusion, and empty sella.

Perioptic nerve sheath distention was defined as CSF collection more than 2 mm in thickness on the coronal T2 weighted images. Buckling or kinking of optic nerve in the vertical direction was seen on sagittal or coronal images. Globe flattening was described as flattening of the posterior aspect of the sclera and optic nerve head protrusion was prominence of the optic nerve head above and beyond the scleral flattening. Both these findings were described on T2 weighted sagittal images, as was the filling of the sella by the pituitary gland. All these imaging features were scored as dichotomous variables (finding present or absent). Images were evaluated in consensus by two neuroradiologists who were blinded to the final diagnosis.

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS, Chicago, IL, USA). Fisher's exact test was used to calculate whether the difference in occurrence of various imaging findings in primary and secondary causes of intracranial hypertension was statistically significant. Odds ratios were also calculated. Subgroup analysis of the IIH versus tumors and IIH versus venous hypertension was performed. A *P* value of less than 0.05 was considered to be statistically significant.

Results

We evaluated five imaging findings as described in 21 patients with proven IIH and 60 patients with secondary intracranial hypertension (41 with tumors; 19 with venous hypertension [17 with venous sinus thrombosis and 2 with dural arterio-venous fistulas]).

The 21 patients in the IIH group had a mean age of 27.6 years (range 7-44 years). All patients but one were females. The opening CSF pressure values were available in 16 patients and ranged from 250 to more than 400 mm of water. The CSF opening pressure in the remainder of the five patients was documented in the medical records as elevated. These patients had also undergone fundoscopic evaluation, which revealed bilateral papilledema in 19 patients. In two patients, secondary optic atrophy was seen.

The 19 patients with venous hypertension had a mean age of 28.4 years (range 2-52 years). Eight patients in this group were males and 11 were females. 17 patients had venous sinus thrombosis and two had dural arterio-venous fistulas.

The 41 patients with tumors had a mean age of 35.2 years (range 5-65 years). Eight patients in this group were males and 11 were females. Histopathology findings were available in 39 patients and were fibrillary astrocytoma (16), meningioma (4), medulloblastoma (3), schwannoma (2), oligoastrocytoma (2) and one each of pilocytic astrocytoma, glioblastoma multiforme, pituitary macroadenoma, hemangioblastoma, ependymoma, teratoma, metastasis, pinealocytoma, pineal region astrocytoma, oligodendroglioma, ganglioglioma, epidermoid.

Of all the imaging findings evaluated, optic nerve head protrusion and globe flattening were significantly associated with IIH ($P = 0.021$ and 0.021, respectively). There was no statistically significant difference in the occurrence of rest of the findings. These results are described in Table 1.

On subgroup analysis [Table 2], globe flattening and optic nerve head protrusion occurred significantly more often in IIH than in tumors ($P = 0.033$ and 0.007, respectively). On comparing patients with IIH and venous hypertension, nerve sheath buckling occurred more frequently in patients with venous

Table 1: Occurrence of findings in idiopathic and secondary hypertension

Findings	IIH (%)	Secondary intracranial hypertension (%)	Fishers exact test (*P* value)	Odds ratio (95% confidence interval)
Perioptic nerve sheath distention	20 (95.2)	50 (83.7)	0.273	0.250 (0.030-2.08)
Vertical buckling of optic nerve	13 (61.9)	35 (58.3)	0.803	0.862 (0.311-2.388)
Globe flattening	15 (71.4)	24 (40)	0.021	0.267 (0.091-0.784)
Optic nerve head protrusion	15 (71.4)	24 (40)	0.021	0.267 (0.091-0.784)
Empty sella	16 (76.2)	41 (68.3)	0.587	0.674 (0.215-2.113)

IIH=Idiopathic intracranial hypertension

hypertension and globe flattening occurred more often in IIH. These findings approached statistical significance (P = 0.069 and P = 0.055, respectively). Representative cases of IIH and secondary intracranial hypertension due to tumor and venous hypertension are described in Figures 1-3, respectively.

Discussion

IIH is now a well-established entity with the diagnostic criteria defined initially by Dandy[1] and modified by Freidman *et al*.[3] These include both clinical and radiologic criteria (absence of hydrocephalus, structural/mass lesions/vascular pathology.[3] The pathophysiology of this condition is still unclear. Due to greater awareness of this condition, this condition is now being diagnosed with increasing frequency. It is crucial to differentiate between idiopathic and secondary causes of raised intracranial tension.[8] Severe IIH may lead to visual deterioration, which can be prevented by optic nerve sheath fenestration. Appropriate treatment can be instituted for secondary causes like venous sinus thrombosis or meningitis.

It is difficult to clinically differentiate between secondary intracranial hypertension and IIH.[8, 9] Historically, the primary role of imaging in the diagnosis of IIH has been to exclude other conditions that can cause increased ICP and papilledema. There have been many attempts in the past to define objective structural signs on cross-sectional imaging that would actually identify IIH patients.

Table 2: Subgroup analysis (Fisher's test)

Findings	IIH versus tumors (*P* value)	IIH versus venous hypertension (*P* value)
Perioptic nerve sheath distention	0.150	0.596
Vertical buckling of optic nerve	0.283	0.069
Globe flattening	0.033	0.055
Optic nerve head protrusion	0.007	0.328
Empty sella	0.562	1.000

IIH=Idiopathic intracranial hypertension

Many articles have described imaging signs of IIH on MRI.[5-7] Most reports regarding this subject conclude that in the appropriate clinical setting, there are several neuroimaging signs that, although not specific, can assist in establishing the diagnosis of IIH.

Lim *et al*.[5] and Agid *et al*.[10] have described the specificity and sensitivity of these imaging findings in IIH. Agid *et al*.[10] have shown that posterior globe flattening, optic nerve sheath distension, optic nerve tortuosity, and empty sella turcica were significantly associated with IIH and posterior globe flattening, optic nerve protrusion and slit like ventricles had maximum specificity (100%). However, none of the signs taken separately or in combination were sensitive. Posterior globe flattening was the only finding that if present was suggestive of the diagnosis of IIH. Lim *et al*.[5] found a similar high specificity for optic nerve head protrusion but lower specificity for flattening of the posterior sclera (60%). They found statistical significance only for optic nerve tortuosity. A recent article by Rohr *et al*.[11] described the MRI findings in secondary intracranial hypertension. They found the most valid signs being cranial venous outflow obstruction and optic nerve sheath hydrops (sensitivity of 94% and 92% and a specificity of 100% and 89%, respectively). In the same study, optic nerve sheath hydrops and decrease in pituitary height discriminated best between patients with intracranial hypertension and controls.

However, these studies compared patients with IIH with normal controls[5,10] or secondary intracranial hypertension with controls.[11] Though the sensitivity and specificity of these signs has been well studied, there is a paucity of literature

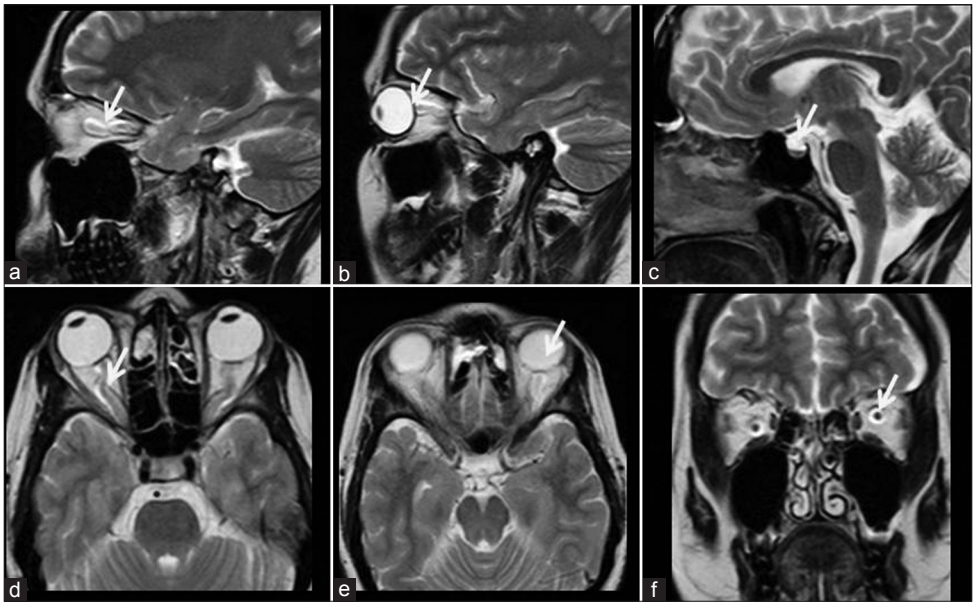

Figure 1: Idiopathic intracranial hypertension – note the T2 weighted images showing the vertical buckling of the optic nerve (a), globe flattening and prominance of the optic nerve head (b, d), partially empty sella (c) and prominent perioptic nerve sheath (d, f)

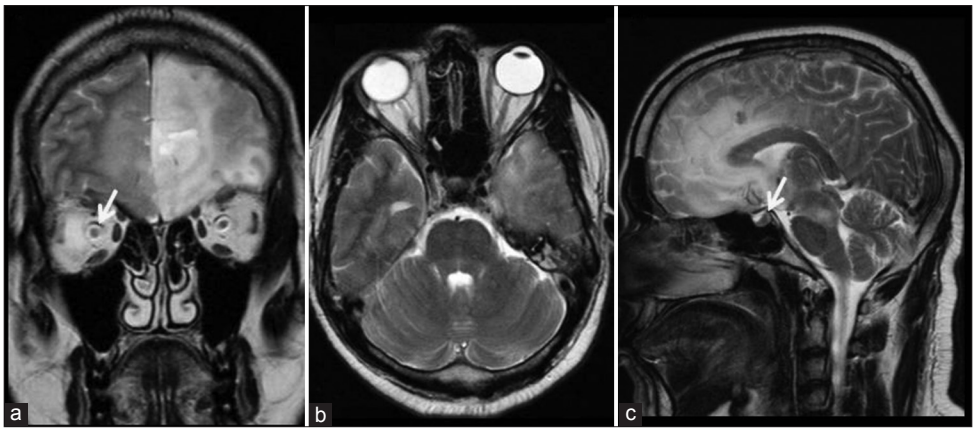

Figure 2: Diffuse fibrillary astrocytoma involving the left frontal lobe with signs of secondary intracranial hypertension – T2 weighted images with prominent perioptic nerve sheath (a), absence of globe flattening (b), and normal appearance of the sella (c)

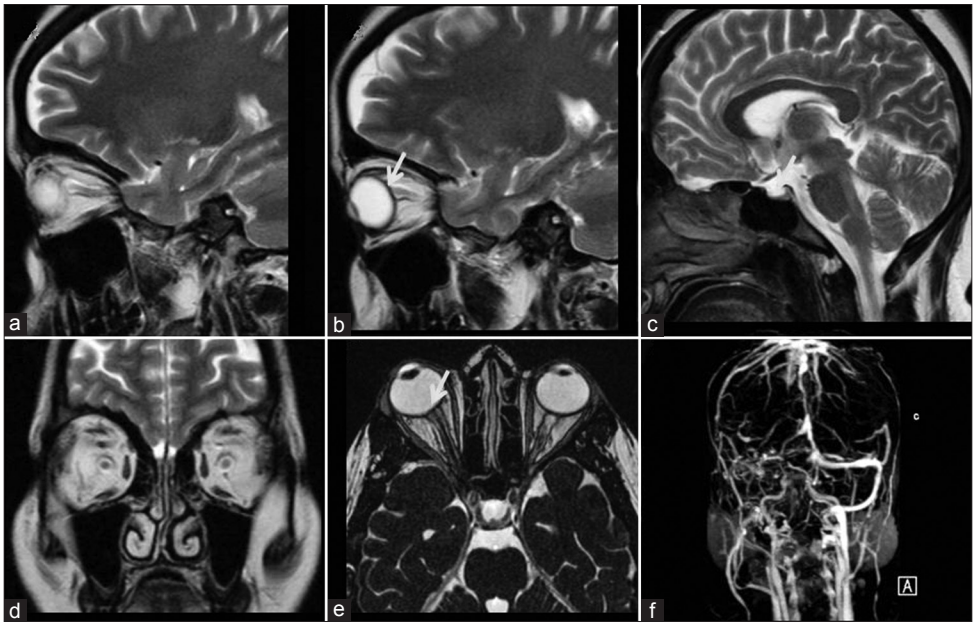

Figure 3: Venous sinus thrombosis involving the right transverse and sigmoid sinuses – no significant vertical buckling of optic nerves (a, b), protrusion of the optic nerve head (b), empty sella (c), prominent perioptic nerve sheath (a, b, d), and globe flattening (e). Magnetic resonance venogram shows non-filling of right transverse and sigmoid sinuses (f)

regarding which of these signs would best differentiate between idiopathic and secondary hypertension. In our study, we compared the incidence of occurrence of various imaging signs on MRI like perioptic nerve sheath distention, vertical buckling of optic nerve, globe flattening, optic nerve head protrusion, and empty sella in patients with IIH and secondary (tumors and venous hypertension) intracranial hypertension.

We found a statistically significant difference in the occurrence of optic nerve head protrusion and globe flattening. There was no statistically significant difference in the occurrence of rest of the findings. Even on subgroup analysis, there was no significant difference except for the occurrence of globe flattening and optic nerve head protrusion more commonly in IIH than in tumors. Thus, only optic nerve head protrusion and globe flattening occurred more commonly in IIH as compared to secondary intracranial hypertension.

Rohr *et al*.[11] correlated the CSF pressure with MRI findings in patients with secondary intracranial hypertension and found significantly higher CSF pressure in patients with optic disc protrusion and optic nerve edema. They also found higher CSF pressure in patients with a greater degree of venous sinus stenosis. However, the optic nerve sheath diameter, height of the pituitary gland and superior ophthalmic vein diameter did not correlate with the ICP.

The limitations of this study include its retrospective nature and the associated bias. A larger prospective study with subgroup analysis would help in this case. Routine imaging performed for brain study (5 mm slices) was evaluated for the presence/absence of various findings. Special imaging of the orbits was not done. This could simulate routine clinical practice where thin sections for orbital imaging may not be available in all cases with raised intracranial tension. Other signs of IIH described in other articles like enhancement of the optic nerve head[10]

and venous sinus stenosis could not be evaluated in our study due to non-availability of contrast enhanced images in all our patients.

Conclusions

While many MRI findings have been reported for IIH, except for optic nerve head protrusion and globe flattening, the majority of these signs of IIH on MRI are not helpful in differentiating between idiopathic and secondary causes of intracranial hypertension.

IIH is a diagnosis of exclusion. While secondary causes of raised ICP have obvious clinical findings on MRI, some conditions like cerebral venous thrombosis may have subtle signs and differentiating between primary and secondary causes may be difficult. In the absence of any evident cause of raised ICP, presence of optic nerve head protrusion or globe flattening can suggest the diagnosis of IIH.

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