The Validity of MRI and MRV in Diagnosis of Pseudotumor Cerebri

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ABSTRACT:

BACKGROUND:

Pseudotumor cerebri (PTC) is an entity of uncertain cause recognized by increased intracranial pressure. The diagnosis rely on clinical symptoms, absence of structural, hydrocephalus, , vascular or intracranial mass lesion on imaging, increased cerebrospinal fluid pressure measured by lumbar puncture, and normal CSF composition. MRI (magnetic resonance image) and MRV (magnetic resonance venography) findings have been reported to be associated with Pseudotumor cerebri.

OBJECTIVE:

To assess the validity of individual magnetic resonance imaging (cross-sectional and venographic) signs associated with PTC and determine whether the gathering of cross sectional magnetic resonance image and magnetic resonance venography findings enhances the PTC diagnostic certainty.

PATIENTS AND METHODS:

It is a case-control study that 30 patients were included with PTC and 41 healthy persons. All participants (patients and controls) were subjected to brain MRI and MRV. MRI evaluated the presence or absence of the reported findings. Studies of MRV were evaluated the stenosis of transverse venous sinuses.

RESULTS:

Showed that partially empty sella had the best sensitivity (90%) with a specificity of 80.5%. Posterior displacement of stalk: had a sensitivity and specificity of 76.67% and 65.85%, respectively. Peri-optic nerve (PON) sheath distention revealed a sensitivity and specificity of 76.67% and 92.68%, respectively, making it one of the best MRI signs. These MRI signs when combined with MRV, the sensitivity and specificity of all signs increased largely.

CONCLUSION:

Three MRI signs; partially empty sella, posterior displacement of stalk, and PON sheath distention strongly suggest the diagnosis of PTC. Using MRV in combination with MRI findings greatly enhances the diagnostic value of all individual MRI findings in the detection of PTC.

KEYWORDS: Pseudotumor cerebri, MRI and MRV.

INTRODUCTION:

Pseudotumor cerebri (PTC) is a clinical syndrome of increased intracranial pressure (ICP) without mass intracranially, tumor, or ventriculomegaly causing signs and symptoms of increase intracranial pressure. composition of cerebrospinal fluid (CSF) is normal. The primary form known as idiopathic intracranial hypertension (IIH), the PTC term is more including of secondary etiologies. IIH is the idiopathic or primary form of PTC usually affects obese women of childbearing age [1]. Many diagnostic criteria for PTC have been proposed, but a diagnosis can usually be confidently made with the **modified Dandy criteria** [2]. Marmarou et al [3]. and Stevens et al [4] models defined stenosis as a reduction in 40% of the diameter of the vessel. While, a sinus that is 40% smaller in average diameter than the contralateral sinus defined as hypoplastic sinus. Clinical presentation can be variable in children and may be less obvious than in their adult counterparts. Papilledema can also be challenging to diagnose in this population. The upper limits for opening pressure on lumbar puncture differ in children, with a cut-off of 25 cm H20 (or 28 cm H2O in a sedated or obese child). [5]. The transverse sinuses are may be asymmetric in most peoples and a unilateral hypoplastic transverse sinus can be considered as a "normal variant" with no changes reported in ICP. MRV

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demonstrated variable degrees of cerebral venous stenosis in most of the PTC cases compared with normal controls [5]. Still there is a doubt on whether such stenosis is the effect or cause of PTC. Some authors argued that the venous sinus theory could not explain the female predominance of PTC in adults [6]. Moreover, the clinical course was not correlated with the degree of TSS especially visual field loss [7]. It has also been suggested that such narrowing is secondary to compression of the sinuses by the raised ICP causing outflow obstruction, which results in more increase in venous pressure, decreases CSF absorption and result in further increase of ICP [8,4]. One Study suggests that PTC may be caused by a sufficiently collapsible transverse sinus, but it is also possible that a stenosed sinus may persist after the resolution of intracranial hypertension [9]. On other hand, some studies that deal with anatomical issues suggested that these stenoses occur due to the presence of septae, trabeculae or hypertrophied granulations within the transverse sinuses [10,11]. A positive feedback mechanism has also been proposed suggesting that venous hypertension leads to further increased ICP, independently of the initial cause of focal stenosis [12]. There are many reported signs on cross-sectional brain MRI imaging that associated with PTC, including posterior globes flattening which is seen in about 80%, intraocular portion protrusion of the optic nerve (ON), vertical tortuosity of the ON in which seen in 40%, ON sheaths distension, partial empty sella turcica which seen in 70%, slit-like ventricles, tight subarachnoid space around the optic nerves which seen in 45%, posterior displacement of the stalk, large Meckel's caves, prominent arachnoid pits and Inferior displacement of cerebellar tonsils [13,14,15,16,17,18]. Two reported similar case control studies estimated the accuracy of previously reported neuroimaging signs in excluding or establishing the diagnosis of PTC. The study of **Agid et al., 2006** found that the majority of the reported signs for PTC on cross-sectional imaging do not help establish or exclude the diagnosis of PTC, and are of no value in the clinical setting. Posterior flattening of the globe is the only sign that, when present, is suggestive of the diagnosis of PTC [18]. **P.J. Maralani et al., 2012** study showed that MRI of brain with venography significantly enhanced the diagnostic certainty for PTC if there was no evidence of hydrocephalus, mass or sinus thrombosis and one of the following signs was present: posterior globes flattening, partially empty sella or combined stenosis score < 4. However, the absence of these signs did not exclude a diagnosis of PTC [19]. The study aims to assess the validity of each MRI imaging (including cross-sectional and venographic) signs associated with PTC. To determine whether the combination of cross-sectional MRI and MRV findings increases the diagnostic certainty for PTC.

PATIENTS AND METHOD:

Study design and setting: This is a case-control prospective study that was performed at the neurology unit of Al-Imamain Al-Kadhimain medical city throughout the period from June - 2019 to December - 2020 over 18 months, where a random selection of PTC patient cases was enrolled.

Patients and Controls: Thirty (30) patients, with a confirmed diagnosis of PTC by neurology consultant had been studied as (patients group) and labelled as cases.

Inclusion criteria: Any new patient diagnosed with PTC and confirmed by clinical, brain imaging, and LP were enrolled in the study.

Exclusion criteria: are as If brain imaging of any patient reveals a mass lesion, venous sinus thrombosis, or hydrocephalus and patient who underwent surgical treatments previously.

Controls: Another 41 patients were enrolled based on the availability of a brain MRI and MRV reported as normal by a neuroradiologist. Unfortunately, no clinical data were available for the controls, because they were collected retrospectively from the archived data based on normal reports, decided to be normal by consensus radiologist opinion.

Data collection: For both groups (patients and controls) a detailed history was revised concerning demographical, clinical, and radiological features, with emphasis on MRI and MRV findings.

Image Protocols: An imaging scan of the brain from the vertex to the base of the skull was performed by Philips healthcare Achieva 3T TX 32CH standard neurovascular coil (8 channel). Routine coronal, axial, and sagittal T2-weighted images (TR=3440–4100 ms; TE=84–88 ms; field of view 23 cm; slice thickness 5mm; interslice gap1mm; echo train length, 16; matrix, 352×256; the number of average=2) and 3DPCA MRV (TR=15ms, TE=35 ms; field of view 22cm; slice thickness 1.4 mm; the number of average 1; echo train length 1; matrix 256*256; flip angle10°) source, and maximum intensity projection (MIP) images were evaluated.

Evaluation and Analysis of Scanned Images: The images were reviewed by experienced neuroradiologists for the following defined findings: (1) partially empty sella turcica (if pituitary gland occupies less than 50% of the pituitary foss); (2) pituitary stalk posterior displacement; (3) posterior globe flattening (flattenning of outward convexity of the sclera at the area of ON attachment; (4) intraocular ON protrusion (concave sclera towards the globe at ON attachment); (5) ON sheath distension (CSF space of ON is greater than 2 mm); (6) ON vertical tortuosity (on sagittal views a "S-shaped" appearance of ON); (7) slit-like ventricles (collapsed lateral ventricles walls); (8) subarachnoid spaces tightness (a very small sulci and cisterns); (9) inferior displacement of cerebellar tonsils (the cerebellar tonsils descent >5 mm); (10) large Meckel's caves; (11) prominent arachnoid pits (are arachnoid granulations that penetrated the dura but failed to migrate normally in the venous sinus). MRV studies were interpreted as negative if both right and left transverse sinuses are patent or one sinus showed smooth hypoplasia, and considered positive if significant unilateral or bilateral venous sinus stenosis was observed. Significant stenosis was defined as focal short or long segment narrowing in the lateral sinus that is less than 50% compared with the distal segment of the superior sagittal sinus.

Statistical analysis:

Statistical Package for Social Sciences (SPSS) software version (25.0) was used for all statistical analyses. For each MRI sign for IIH, a two-by-two table of disease status by the presence of the sign was created. The sensitivity, specificity, likelihood ratio positive (LR+), and likelihood ratio negative (LR−) were also calculated to measure the diagnostic strength of the sign. A p-value ≤ 0.05 was considered statistically significant.

RESULTS:

Demographic Characteristics of the Study population:

The mean age of the patients was 32.73±8.67 years (range 16-47 years) which was lower than that of controls (mean= 42.32±16.29 years, range 15-77 years) with a significant difference. The vast majority of patients (27, 90%) were females, while there were only three males (10%). While in controls males and females were almost equally distributed (51.22% and 48.78%, respectively), with a significant difference between patients and controls.

MRI Findings in Patients and Controls:

Eleven MRI findings besides MRV were included in this study. The frequencies showed in table 1 :

Table 1: The prevalence of MRI findings among 30 patients and 41 controls.

MRI findings	Patients with findings		Controls with findings		p-value
	No.	%	No.	%	
Partially empty sella	27	90.0	8	19.51	<0.001
Posterior displacement of stalk	23	76.67	14	34.15	<0.001
Peri-optic nerve sheath distention	23	76.67	3	7.32	<0.001
Vertical tortuosity of ON	16	53.33	2	4.88	<0.001
Flat posterior globe	15	50.0	2	4.88	<0.001
Large Meckel's caves	10	33.33	3	7.32	0.005
Intra-ocular protrusion of ON	8	26.67	0	0.0	<0.001
Slit like ventricles	7	23.33	1	2.45	0.006
Tight subarachnoid space	4	13.33	1	2.45	0.076
Prominent arachnoid pits	4	13.33	3	7.32	0.403
Inferior displacement of cerebellar tonsils	1	3.33	0	0	0.239
MRV	28	93.33	4	9.76	<0.001

Diagnostic Value of MRI Findings:
The sensitivity and specificity of each signs showed in table 2 :

Table 2: Statistical parameters of individual imaging findings.

MRI findings	Sensitivity	95%CI	Specificity	95%CI	+LR	-LR
Partially empty sella	90.0	85.22-94.78	80.5	76.63-34.37	4.61	0.124
Posterior displacement of stalk	76.67	72.21-81.13	65.85	62.35-69.35	2.25	0.356
Peri-optic nerve sheath distention	76.67	72.21-81.13	92.68	95.68-100	10.47	0.253
Vertical tortuosity of ON	53.33	49.61-57.05	95.12	88.52-96.84	10.93	0.49
Flat posterior globe	50.0	46.4-53.6	95.12	91.62-100	10.24	0.525
Large Meckel's caves	33.33	30.4-36.26	92.68	88.52-96.84	4.55	0.719
Intra-ocular protrusion of ON	26.67	24.05-29.29	100	90.91-99.33	53.34	0.734
Slit like ventricles	23.33	20.89-25.77	97.56	90.91-99.33	9.52	0.787
Tight subarachnoid space	13.33	11.5-15.16	97.56	93.3-100	5.44	0.889
Prominent arachnoid pits	13.33	11.5-15.16	92.68	88.52.98.84	1.82	0.936
Inferior displacement of cerebellar tonsils	3.33	2.47-4.19	100	93.3-100	6.66	0.667
MRV	93.33	88.4-98.26	90.24	86.14-94.34	9.56	0.078

Diagnostic Value of the Combination of MRI Findings with MRV:
When combined with MRV, the sensitivity and specificity of all MRI signs increased largely as shown in table 3:

Table 3: Statistical parameters of a combination between MRV and individual imaging findings.

MRI findings	Sensitivity	95%CI	Specificity	95% CI
Peri-optic nerve sheath distention	100	94.9-100	97.56	93.3-100
Partially empty sella	96.67	91.66-100	100	95.68-100
Posterior displacement of stalk	96.67	91.66-100	97.56	93.3-100
Intra-ocular protrusion of ON	96.67	91.66-100	100	95.68-100
Vertical tortuosity of ON	93.33	88.4-98.26	100	95.68-100
Slit like ventricles	93.33	88.4-98.26	100	95.68-100
Tight subarachnoid space	93.33	88.4-98.26	100	95.68-100
Inferior displacement of cerebellar tonsils	93.33	88.4-98.26	100	95.68-100
Prominent arachnoid pits	93.33	88.4-98.26	92.68	88.52-96.84
Flat posterior globe	90	85.16-94.84	100	95.68-100
Large Meckel's caves	90	85.16-94.84	95.12	90.91-99.33

DISCUSSION:

According to the results of the study, patients had significantly lower mean age than controls while the frequency of females was much higher in patients than controls with a significant difference. Such results were reported in a previous study [19,21], and it is assumed to not affect the occurrence of MRI signs between the patients and controls, as the signs of interest were unlikely to be related to age or gender. This was confirmed by logistic regression analyses in a previous study that examined the relationship between the occurrence of signs on MRI and both age and gender [19]. In the current study, MRI findings including empty sella, posterior displacement of stalk, PON sheath distention, vertical tortuosity of ON, flat posterior globe, intra-ocular protrusion of ON, large Meckel's caves, and slit-like ventricles were significantly associated with PTC, while tight subarachnoid space, inferior displacement of cerebellar tonsils and prominent arachnoid pits had no significant association with PTC. In a similar study, Agid et al. [19] the distension of ON sheath, tortuosity of ON, flattening of posterior globe, pituitary deformity, and partially empty sella turcica were significantly associated with PTC, ON protrusion and enhancement, slit-like ventricles, and tight cerebrospinal fluid spaces were not significantly associated with PTC.

In Canada, Maralani et al. [20] evaluated the accuracy of individual and combinations of signs on brain MRI and MRV in the diagnosis of PTC. Seven signs found to be more prevalent in PTC patients versus control subjects in the study; ON protrusion , empty sella, posterior displacement of the pituitary stalk, posterior globe flattening, distension of ON sheath, ON vertical tortuosity, and bilateral sever TSS. Many other studies demonstrated variable findings. In three studies, the ON sheaths were found to be significantly wider in PTC patients compared with controls [22,23,24]. One study showed that an elongated, enlarged subarachnoid space surrounding the ON was more common in PTC patients than in healthy controls, but did not found to be statistically significant [25]. Posterior globe flattening was reported to be significantly more prevalent in PTC patients [24]. These differences between the studies are justifiable and may be attributed to the differences in sample size, retrospective nature of some of them, and variation of inter-observer in the reading of MRI. As far as there is a clear disparity in the significance of MRI signs in different trials; the present study aimed to assess the sensitivity, specificity, and reliability of individual MRI imaging (cross-sectional and venographic) signs associated with PTC then assess the yield of combined the MRV sign with the most significant MRI signs. According to the results of the present study, three MRI signs: partially empty sella, posterior displacement of stalk, and PON sheath distention strongly suggest the diagnosis of PTC with a sensitivity of 90%, 76.67%, and 76.67%, respectively, and specificity of 80.5%, 65.85%, and 92.68%, respectively, while all other signs had low sensitivity in general. Similarly, Maralani et al. [20] stated that three signs were of sufficient diagnostic value of PTC. These were partially empty sella (specificity 95.3%), posterior globes flattening (specificity 100%), and combined stenosis score (CSS) < 4 (specificity 100%). Brodsky and Vaphiades [26] discovered a sensitivity and specificity of 80% and 95% for posterior globes flattening and 70% and 95% for empty sella, respectively. In Turkish study reported that posterior globe flattening had 64% sensitivity, 100% specificity, distention of ON, 46% sensitive, 100% specific), empty sella (43% sensitive, 100% specific), and ON vertical tortuosity (30%sensitive, 95% specific), The difference in rates reported between studies may in part relate to differing patient and control populations, differing definitions of stenosis, or possibly the parameters used in MRV and utilized technique. All studies included had a case-control design, which may have resulted in the overestimation of diagnostic accuracy [27]. And, the healthy controls inclusion could lead to a further specificity overestimation. For the MRI sign “distension of ON sheath ", in studies using "normal" volunteer had a diagnostic performance significantly higher than in studies using patients with normal brain MRI findings as control subjects [28]. The sensitivity and specificity of all MRI signs in the current study increased significantly when combined with MRV. This is following the study of Maralani et al. [20] who reported that a combination of brain MRV with MRI significantly enhanced the diagnostic certainty for PTC if there was no evidence of hydrocephalus, mass, or sinus thrombosis. Thus, a combination of MRV with MRI findings can greatly enhance the diagnostic value of individual MRI findings. Finally, Maralani et al. [20] stated that the absence of MRI or MRV signs did not exclude PTC as 14% of their patients had PTC with no MRI/MRV signs, while in the present study all patients who were diagnosed with PTC had either MRI or MRV signs with 100% sensitivity in the diagnosis of PTC. This difference can be explained by strict criteria which have been followed in their study to calculate sinus stenosis, the right and left transverse sinuses in which assigned score based on the median value of the three readers. Moreover, a calculated combined stenosis Score as the sum of the right and left transverse sinus stenosis grades. Also, for sensitivity and specificity calculations, a positive imaging findings were considered only if findings are identified by two of the three neuroradiologists readers. And likewise all these criteria were not followed in the current study.

CONCLUSION:

1. Three MRI signs: partially empty sella, posterior displacement of stalk, and peri-optic nerve sheath distention strongly suggest the diagnosis of PTC with a sensitivity of 90%, 76.67%, and 76.67%, respectively, and specificity of 80.5%, 65.85%, and 92.68%, respectively, could be used as supportive findings in the diagnosis of PTC, while the other reported signs are of minimal or no

value in evaluating the individual patient for the possible diagnosis of PTC.

2. Using MRV in combination with MRI findings greatly enhances the diagnostic value of all individual MRI findings in the detection of PTC.

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