Parkinsonism and Related Disorders 20 (2014) 180–185

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

The pimple sign of progressive supranuclear palsy syndrome

Hugo Botha [a], Jennifer L. Whitwell [b], Ajay Madhaven [b], Matthew L. Senjem [c], Val Lowe [b], Keith A. Josephs [a,*]

[a] Department of Neurology, Mayo Clinic, Rochester, MN, USA
[b] Department of Radiology, Mayo Clinic, Rochester, MN, USA
[c] Department of Information Technology, Mayo Clinic, Rochester, MN, USA

ARTICLE INFO

Article history:
Received 2 August 2013
Received in revised form
12 October 2013
Accepted 25 October 2013

Keywords:
Midbrain atrophy
PSPS
FDG-PET
Pimple sign
Parkinsonism

ABSTRACT

Background: Some patients with progressive supranuclear palsy syndrome (PSPS) demonstrate a focal area of midbrain hypometabolism on FDG-PET scans which we call the 'pimple sign'. We assessed its association with midbrain atrophy, its reliability and its ability to differentiate PSPS from corticobasal syndrome (CBS) and multiple system atrophy (MSA).
Methods: We identified 67 patients with PSPS, CBS or MSA who had volumetric MRI as well as FDG-PET imaging. Midbrain volume was measured and expressed as a percentage of total intracranial volume. Two independent, blinded specialists rated the 'pimple sign' on FDG-PET as 'absent', 'possible' or 'definite'. Midbrain volumes were compared across these groups and reliability assessed with the kappa statistic. Sensitivity and specificity were calculated using CBS and MSA patients as controls.
Results: Midbrain volume was decreased in the 'definite' group compared to the 'absent' and 'possible' groups ($p = 0.0036$). Inter-rater reliability for the pimple sign was high ($\kappa = 0.90$). A 'definite pimple sign' had a high specificity (100%) but low sensitivity (29%) for PSPS, whilst the presence of a possible or definite sign had a sensitivity of 79%.
Conclusion: The 'pimple sign' of PSPS is associated with midbrain atrophy, and may be helpful in differentiating PSPS from CBS and MSA.

© 2013 Elsevier Ltd. All rights reserved.

1. Introduction

Progressive supranuclear palsy (PSP) is a chronic, progressive neurodegenerative disorder characterized pathologically by the accumulation of abnormal tau protein [1]. In its typical form, PSP syndrome (PSPS), it manifests clinically with postural instability, vertical supranuclear gaze palsy, axial rigidity and dysarthria, although a large spectrum of other presentations can be associated with PSPS [2]. Diagnosing PSPS can be very challenging, especially given the significant overlap with other atypical parkinsonian disorders [3]. In addition to the need for accurate diagnosis and prognosis, differentiating it from other degenerative disorders will become increasingly important as disease modifying treatments become available.

Neuroimaging can aid in the early diagnosis of PSP. Magnetic resonance imaging (MRI) findings that have been described in PSPS include atrophy of the midbrain, superior cerebellar peduncle and frontal lobes [4,5]. Midbrain atrophy can often be seen on visual inspection, as the "hummingbird sign" on sagittal view of the brainstem [6]. Several midbrain-related indices, involving midbrain diameter, area and volume have been described, with varying clinical utility [7,8].

Positron emission tomography (PET) imaging with 18F-fluorodeoxyglucose (FDG) has been shown to be helpful in differentiating among parkinsonian disorders. Characteristic metabolic abnormalities in PSPS include hypometabolism of the brainstem and midline frontal structures, although brainstem hypometabolism has been observed in corticobasal degeneration (CBD) or multiple system atrophy (MSA) [9]. Midbrain hypometabolism could be a promising early marker of PSPS, but isn't readily apparent on visual inspection of conventional PET images [10]. Several software packages allow for the creation of metabolic maps for each patient using Z-scores, after which metabolism can be assessed visually, and CortexID is used at our institution [9]. The use of such automated statistical analyses has made FDG-PET a more feasible clinical tool, and increases the sensitivity and specificity of FDG-PET [9,11].

We have noticed a focal area of midbrain hypometabolism on CortexID FDG-PET scans in some patients with PSPS and have

* Corresponding author. Mayo Clinic, 200 1st St SW, Rochester, MN 55905, USA. Tel.: +1 507 538 1038; fax: +1 507 538 6012.
E-mail address: josephs.keith@mayo.edu (K.A. Josephs).

1353-8020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.parkreldis.2013.10.023

named this the 'pimple sign'. It is unclear, however, how this relates to midbrain atrophy, as prior research suggests midbrain hypometabolism is present early, doesn't progress as much as other areas of hypometabolism and doesn't correlate with clinical deterioration, whereas it is clear that midbrain atrophy progresses in a near-linear fashion in PSPS and correlates with disease progression [10,12]. Whether the pimple sign is indicative of midbrain atrophy or associated with PSPS has not been established. Our primary objective was to assess whether the pimple sign is associated with midbrain atrophy. Our second objectives were to determine inter-rater reliability of the sign and to assess whether the pimple sign is associated with PSPS.

2. Methodology

2.1. Subjects

The Mayo Clinic Medical Records Linkage system was queried to identify all patients seen in the Department of Neurology between January 1, 2005, and September 30, 2012 who had a clinical diagnosis of PSPS, CBS or MSA and had both volumetric MRI as well as FDG-PET imaging done within 12 months of each other. The following search terms, along with their abbreviated versions, were used: *progressive supranuclear palsy*, *Richardson syndrome*, *Steele–Richardson–Olszewski syndrome*, *multiple system atrophy*, *multisystem atrophy*, *corticobasal degeneration*, *corticobasal ganglionic degeneration* and *corticobasal syndrome*. A total of 89 patients were identified. Patients were retrospectively diagnosed at the time they were imaged, according to the NINDS-SPSP criteria for PSPS [13], the criteria for CBS [14] and the criteria for MSA [15]. Patients where the diagnosis was strongly suspected clinically but where patients didn't meet criteria for any of the disorders at the time of their scans were excluded. Cases which met criteria for both possible PSPS and CBS were designated as possible PSPS (7 patients) given the high specificity of the NINDS-SPSP criteria [16]. Twenty-two patients were excluded because they did not meet criteria for PSPS, CBS or MSA at time of imaging. The clinical records of the remaining 67 patients were reviewed to extract clinical data, including age at onset, age at scan, sex, initial presenting symptoms, dates of MRI and PET imaging.

The study was approved by the Mayo institutional review board.

2.2. FDG-PET imaging

All PET scans were acquired using a PET/CT scanner (GE Healthcare) operating in 3D mode. Subjects were injected with fluorodeoxyglucose in a dimly lit room with minimal auditory stimulation. An 8-minute FDG scan was performed after a 30-minute uptake period, which consisted of four 2-min dynamic frames following a low dose CT transmission scan. Standard corrections were applied and frames were realigned if motion was present. We used the CortexID (GE Healthcare) software package and ran an automated analysis using 3D stereotactic surface projections [17]. Activity for each subject's scan was normalized to the pons and compared to an age-segmented normative database. The program provides 3D stereotactic surface projection images with a metabolic map using the Z-scores as calculated for each surface pixel. The midsagittal images were extracted for analyses since we were interested only in the midbrain. Two experts (KAJ and JLW), blinded to patients' clinical information as well as midbrain data, independently rated the scans as showing an 'absent', 'possible' or 'definite' pimple sign (See Fig. 1). Grading was done focusing only on that one area independent of hypometabolism elsewhere throughout the brain. Their responses were recorded and discordant cases were discussed and a consensus reached.

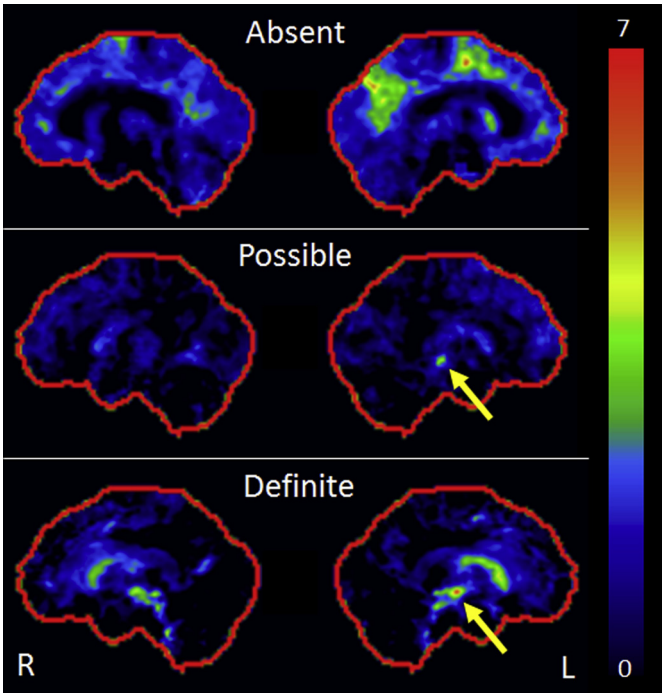

Fig. 1. FDG-PET imaging showing examples of 'absent', 'possible' and 'probable' pimple signs.

2.3. Volumetric MRI

All patients had a volumetric MRI performed with a standardized protocol, as previously described [18]. Midbrain volume was measured for each scan by propagating a template-drawn midbrain volume mask into the native space of each patients scan. Midbrain volume was manually traced on a customized template in Analyze software (Biomedical Imaging Resource, Mayo Clinic, Rochester, MN) according to previously published guidelines [19]. Total intracranial volume (TIV) was measured on each scan by propagating a template-drawn TIV mask to subject space using SPM5. Midbrain volume was divided by TIV (MB/TIV) in order to correct for differences in head size across subjects [20].

2.4. Statistical analysis

JMP Pro Version 9.0.3 (SAS Institute Inc, Cary, NC, USA) was used for all the statistical analyses, with alpha set at 0.05. One-way ANOVA was computed using the MB/TIV variable across the 'absent', 'possible' and 'definite' groups, and since this showed statistical significant differences, comparison of each pair using Student's t was computed. The Bonferroni correction for multiple comparisons was applied. Inter-rater reliability was assessed with the kappa statistic. The sensitivity and specificity of a 'definite' as well as 'possible' pimple sign were assessed by using possible and probable PSPS patients as cases and all other diagnoses as controls. Likelihood ratios were computed, correcting for empty cells in the 2×2 table by adding 0.5 to all cells [21].

3. Results

3.1. Patient characteristics

Demographic characteristics are summarized in Table 1 and the final diagnoses in Table 2. Of note, among the three groups

Download English Version:

https://daneshyari.com/en/article/10745580

Download Persian Version:

https://daneshyari.com/article/10745580

Daneshyari.com