Clinical Neurology and Neurosurgery 115 (2013) 1040–1043

Contents lists available at SciVerse ScienceDirect

Clinical Neurology and Neurosurgery

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

Brain white matter hyperintensities in migraine: Clinical and radiological correlates

Udaya Seneviratne[a,*], Winston Chong[b], P.H. Billimoria[c]

[a] Department of Neuroscience, Monash Medical Centre & Monash University, Clayton, VIC 3168, Australia
[b] Department of Diagnostic Imaging, Monash Medical Centre, Clayton, VIC 3168, Australia
[c] Department of Neuroscience, Alfred Hospital, Prahran, VIC 3181, Australia

ARTICLE INFO

Article history:
Received 4 May 2012
Received in revised form 28 August 2012
Accepted 28 October 2012
Available online 20 November 2012

Keywords:
Migraine disorders
Magnetic resonance imaging
Stroke
White matter hyperintensity

ABSTRACT

Objective: Migraine is a recognised cause of brain white matter hyperintensities (WMHs) on magnetic resonance imaging (MRI). However radiological characteristics of those in migraine are not well defined. We sought to study the radiological characteristics and factors associated with WMH in migraine.
Methods: Migraine patients who were investigated with MRI of the brain in the outpatient clinic were studied retrospectively. Two groups were delineated based on the presence or absence of WMH in MRI scans. The clinical and demographic characteristics between the two groups were compared to delineate the associations of WMH.
Results: Forty four patients were studied, out of which 19 demonstrated WMH on MRI. Frontal lobe was involved in all subjects with WMH. Infratentorial hyperintensities were not seen in any. Subcortical and deep white matter was the commonest distribution while callosal and subcallosal lesions were very rare. Family history of migraine, increasing age, and increasing headache frequency emerged as significant associations of WMH in multivariable analysis.
Conclusions: There are characteristic radiological features and clinical associations of WMH in migraine.

1. Introduction

Migraine is a common neurological disorder. In the United States, the prevalence has been found to be 17.1% in females and 5.6% in males [1]. Migraine with aura is considered to be a risk factor for ischaemic stroke in females [2]. Brain white matter hyperintensities (WMHs) on magnetic resonance imaging (MRI) have been described in several neurological disorders including ischaemia, multiple sclerosis (MS), and migraine [3].

A population-based, case–control study found that females with migraine had a significantly increased risk of WMH in the brain, independent of migraine subtype and cardiovascular risk factors [4,5]. The same study demonstrated that subclinical infarcts were more frequent in the posterior circulation territory among migraineurs in comparison to controls. From the same cohort, Kruit et al. found infratentorial hyperintensities among 4.4% of migraineurs compared to 0.7% of controls [6]. In a prospective study involving migraineurs with aura, WMH were found in the periventricular region in 19% and deep white matter in 47%, whilst 86% of deep white matter hyperintensities were located within the frontal lobes [7]. Dinia et al. have demonstrated in a longitudinal study that WMH tend to progress over time in migraine patients with aura [8]. Overall, there is a large body of evidence suggesting that patients with migraine, both with and without aura, are at a higher risk of developing subclinical white matter lesions in the brain [5].

Despite the body of literature on this rather complex link between migraine, ischaemia and WMH, information is scant in some areas. First, the relative distribution of the brain WMH load in migraine is not clearly delineated in the literature. Second, the practically relevant question of differentiating WMH of migraine from MS has not received adequate emphasis. Hence it would be of interest to ascertain whether these WMH would fulfil the radiological diagnostic criteria in MS. Against this backdrop, the current study was conducted to describe the radiological characteristics and clinical associations of WMH in migraine. We also sought to test the MRI diagnostic criteria of MS in WMH of migraine in order to assess the chance of diagnostic error.

2. Materials and methods

This is a retrospective study which was approved by the Human Research Ethics Committee of the institute. Medical records of all patients with migraine treated by two neurologists (US and PHB) in their outpatient clinics from January 2003 to June 2007 were screened. The diagnosis had been made based on the International

* Corresponding author. Tel.: +61 3 9594 2240; fax: +61 3 9594 6241.
E-mail addresses: udaya.seneviratne@monash.edu, wusenevi@optusnet.com.au (U. Seneviratne).

0303-8467/$ – see front matter.
http://dx.doi.org/10.1016/j.clineuro.2012.10.033

Headache Society diagnostic criteria [9]. Patients with migraine who had MRI brain scans done as part of their evaluation were selected for the study. MRI was not routinely done in all migraine patients; hence those without MRI scans were not included. Subjects with a confirmed history of stroke or transient ischaemic attack were excluded.

The imaging was performed with a 1.5 Tesla MRI machine (GE Healthcare, UK). The scanning protocol included fluid attenuated inversion recovery (FLAIR) images with a 256×192 pixel matrix and diffusion-weighted imaging. The slice thickness was 5 mm with a gap of 2 mm. Intravenous contrast was not used in any of the cases.

All MRI scans were reviewed and scored by a consultant neuroradiologist (WC) who was blinded to the clinical details. The distribution of WMH (cortical vs subcortical and anatomical regions) was carefully visually assessed by the neuroradiologist. The number of the WMH were counted on the FLAIR images and grouped according to the location and the distribution. Four subgroups were delineated according to the distribution of the WMH following the methodology described by Barkhof et al. in multiple sclerosis patients [10]. These subgroups are juxtacortical, subcortical/deep white matter, callosal/subcallosal and periventriclar. The locations of the WMH were delineated as frontal, temporal, parietal, occipital, and infratentorial. Based on the number of WMH, five subgroups were identified; 0, 1–3, 4–8, ≥9, and confluent. The McDonald MRI diagnostic criteria for dissemination in space in multiple sclerosis [11] were applied to each patient to see whether they fulfil it.

Researchers have previously used different techniques of describing WMH. Rossato et al. used Fazekas scale and Schelten's scale [7]. Semiquantitative scales such as Schelten's were also used by Kruit et al. [4]. Dinia et al. described the WMH distribution based on the topographic territories of brain blood supply [8]. We opted for the Barkhof method with the primary aim of applying MS diagnostic criteria in our cohort.

The demographic and clinical data were collated from the medical records. Data analysis was performed using the SPSS statistical software (SPSS Inc., Chicago, IL, USA). Summary statistics included mean, median, standard deviation (SD), maximum and minimum for continuous variables and percentages as well as frequencies for categorical variables.

In order to find out the factors associated with WMH, multivariable analysis was performed with multiple logistic regression method. The presence or absence of WMH in the MRI was selected as the binary outcome variable. The predictor variables used in the analysis were gender, type of migraine (with or without aura), presence or absence of vascular risk factors (diabetes, hypertension, hyperlipidaemia, smoking), presence or absence of family history of migraine, duration of migraine history (in years) and the number of days with headache per month. The number of headache days per month was obtained around the period the MRI scan was performed. In some patients this information was available in the form of headache diaries. In others, the authors had to depend of the estimate provided by the patients. Odds ratio (OR) with 95% confidence interval (CI) and p value for each predictor variable were estimated. p values of <0.05 were considered statistically significant.

3. Results

A total of 44 patients were studied. There were 37 (84%) females and 7 (16%) males in this cohort with a mean age of 44.7 years (range 19–67). 18 patients (41%) had migraine with aura and visual aura was the most common reported in 15 cases. Family history of migraine was reported by 21 (48%). The mean number of days with headache per month was found to be 12. At least one vascular risk factor was present in 19 (43.2%). The differences between those with and without WMH are summarised in Table 1. WMH on MRI brain scans were detected in 19 (43%). Those were discrete patchy lesions or confluent lesions. All patients had WMH in the frontal lobe while subcortical and deep white matter abnormalities were seen in all abnormal MRIs (Table 2). Four patients (9%) fulfilled McDonald diagnostic criteria of multiple sclerosis (MS) for dissemination in space on MRI. There were no patients with connective tissue diseases in the cohort.

In the multiple logistic regression analysis only 3 variables emerged as factors associated with WMH in migraine. Increasing headache frequency was highly significant with a p value of 0.004 (OR 1.26, 95% CI 1.08–1.48). Those with a family history of migraine were over 50 times more likely to have WMH (OR 52.95, 95% CI 1.94–1442.79, p 0.019). Increasing age was the third association (OR 1.2, 95% CI 1.02–1.41, p 0.031).

4. Discussion

In this study, we have demonstrated that WMH in migraine mostly involve the frontal lobe. Infratentorial and cortical hyperintensities were not seen in our cohort. Callosal and subcallosal lesions were very rare. Increasing headache frequency, increasing age, and positive family history of migraine were clinical associations of WMH. A minority of patients fulfilled the radiological criteria of dissemination in space in MS.

WMH in migraine has been a focus of debate. There has been conflicting evidence with studies demonstrating both increased [12,13], and equal [14], prevalence of WMHs in migraine patients compared with controls. However, a meta-analysis found a higher risk for WMH among patients with migraine (OR 3.9, 95% CI 2.26–6.72) [15]. Furthermore, there is evidence for higher prevalence of posterior circulation territory infarcts among patients with migraine [5].

This study describes the MRI characteristics of WMH in migraine in detail. Frontal lobe is the most likely region to be involved followed by parietal, temporal, and occipital lobes. No subject had WMH in the posterior fossa. In terms of distribution, subcortical and deep white matter hyperintensities are the most common. Callosal and subcallosal lesions are extremely rare but juxtacortical hyperintensities are not uncommon. The majority (63%) has multiple (≥9) hyperintensities.

Table 1
Differences between migraine patients with and without WMH in MRI brain scans.

	MRI without WMH (total 25)	MRI with WMH (total 19)
Mean age (years)	40.6	50.1
Gender	Female 21, male 4	Female 16, male 3
Mean headache frequency (days per month)	7.6	16.9
Mean duration of migraine history (years)	15.1	11.6
Positive family history of migraine	8 (32%)	13 (68.4%)
Migraine with aura	14 (56%)	12 (63.2%)
Migraine without aura	11 (44%)	7 (36.8%)
Presence of vascular risk factors	6 (24%)	13 (68.4%)

WMH, white matter hyperintensities; MRI, magnetic resonance imaging.