Accepted Manuscript

Title: The Value of Patient Directed Brain MRI Scan with a Diagnosis of Migraine

Author: William J. Mullally, Kathryn E. Hall

PII: S0002-9343(17)31124-5
DOI: https://doi.org/10.1016/j.amjmed.2017.10.042
Reference: AJM 14370

To appear in: *The American Journal of Medicine*

Please cite this article as: William J. Mullally, Kathryn E. Hall, The Value of Patient Directed Brain MRI Scan with a Diagnosis of Migraine, *The American Journal of Medicine* (2017), https://doi.org/10.1016/j.amjmed.2017.10.042.

The Value of Patient Directed Brain MRI Scan with a Diagnosis of Migraine

William J. Mullally, M.D. FAHS
Associate Chief of Clinical Neurology
Brigham and Women's Faulkner Hospital
Assistant Professor of Neurology
Harvard Medical School

Kathryn E. Hall, MS, ANP-BC, NE-BC
Nurse Director
Translational and Clinical Research Centers Massachusetts General Hospital
Assistant Professor
MGH Institute for Health Professions

Address all correspondence to:
William J. Mullally, M.D.
1153 Centre Street, 4C
Boston, MA 02130
wmullally@bwh.harvard.edu

Conflict of Interest: None
Both of the authors had access to the data and were involved in writing the manuscript.
Funding: None

Key Words: Brain MRI in Migraine; Migraine; Brain abnormalities in migraine; Brain MRI; Patient directed health care

ABSTRACT

Objective: To determine if a brain MRI scan in patients with a diagnosis of migraine, who insist on the performance of imaging, is of more benefit in detecting clinically significant unsuspected structural abnormalities than would be expected by chance.

Methods: This prospective, observational, single center study was performed from January 1, 2010 to December 31,2012 and included 100 subjects with a diagnosis of migraine and a normal neurologic exam. A brain MRI scan was performed on all patients, solely at their request, to detect an unsuspected clinically significant structural lesion.

Results: Of the 100 patients, 86 were female and the average age was 31.5. 45 patients experienced migraine without aura, 41 with chronic migraine and 14 with migraine with aura. All of the patients had a normal neurologic exam. The duration of headaches ranged from 4 months to 40 years. 82 of the MRI scans were normal and 17 revealed clinically insignificant abnormalities. 1 MRI in a patient with chronic migraine without aura revealed a meningioma that subsequently required surgery and radiation therapy. The 1% prevalence of tumor in this study was then compared to 2 large cohorts of MRI abnormalities in the general asymptomatic population where tumor was found in 35 out of 3000. Fisher's exact test was used to compare the prevalence of tumor in the study population with the combined cohorts and there was no statistical difference between these rates with a p-value of > 0.99.

Conclusions:

Brain MRI obtained at the specific request of patients with a diagnosis of migraine in the presence of a normal neurologic exam has a yield that is equivalent to that of the general asymptomatic population. Patients do not appear to have more insight than the examining clinician with regard to detecting underlying structural abnormalities and brain MRI should not performed as part of the routine evaluation of migraine without a clear clinical indication.

CLINICAL SIGNIFICANCE

More than 1 billion dollars each year are spent on unnecessary brain imaging in the evaluation of headache.

Patients with migraine frequently insist on brain imaging without a clear clinical indication because of the fear of an underlying structural cause.

The chance of finding a brain abnormality in a patient with migraine and a normal neurologic exam is identical to what would be expected in the asymptomatic general population.

INTRODUCTION

Headache is consistently one of the most common complaints for which patients seek medical attention accounting for approximately 1.2% of all outpatient visits[1]. The diagnosis, which usually conforms to one of the primary headache disorders, can almost always be made by a detailed history and neurologic exam. Testing, including imaging of the brain, is only indicated when a secondary headache is suspected. Patients who suffer from headaches are universally concerned about the underlying possibility of structural disease such as tumor or aneurysm and very often that is the primary reason for seeking medical care. A significant number remain concerned despite assurances that they are suffering from a primary headache disorder, including migraine or tension type headache, and insist on a brain imaging study to allay their fears. Patients are often dissatisfied with their care if a scan is not performed even after being reassured about their diagnosis by a headache specialist. The overall yield of brain imaging in patients with a normal neurologic exam and non acute headache is quite low[2]. The prevalence of deep white matter hyperintensities in migraine is relatively high, however, there is no data that indicates that the abnormalities have any long term clinical significance[3,4,5]. Studies have not revealed a higher prevalence of cerebral aneurysms, vascular malformations, or tumors in migraineurs[2,5,6]. Incidental findings on brain imaging lead to additional testing and with the inexorable rise in medical costs it is imperative that we eliminate unnecessary procedures. That, however, must be balanced by providing the best possible care for our patients. The purpose of this study was to determine if patients with a clear history of migraine and a normal neurologic exam had any more insight than the examining clinician in detecting a clinically significant underlying structural brain lesion.

SUBJECTS AND METHODS

STUDY DESIGN: This is a prospective observational, single center, case-control study.

STUDY POPULATION: Approval for this study was obtained from the Harvard Pilgrim Health Care Institutional Review Board. We included 100 consecutive patients, ages 18-64, from January 1, 2010 to December 31, 2012 diagnosed with migraine by International Classification of Headache Disorders-2nd edition criteria[7]. All patients were recruited from the Department of Neurology at Harvard Vanguard Medical Associates in Massachusetts, examined by a neurology provider and had a normal neurologic exam.

Patients were informed of their diagnosis and were told that an imaging study of the brain was not clinically indicated. Despite those assurances the patients insisted that a brain MRI be performed.

BRAIN MR IMAGING: All patients underwent brain MRI with a 1.5T GE scanner including sagittal and axial FLAIR images, axial and sagittal T1, axial T2 weighted, susceptibility and diffusion weighted images. Scans were interpreted by a board certified radiologist with added qualification in neuro-radiology.

STATISTICAL ANALYSIS: We calculated the prevalence of incidental brain abnormalities and compared the data to 2 large studies that examined the prevalence of incidental findings in the general population. Incidental findings were considered significant

if they required treatment or intervention specific to the abnormality.

RESULTS

The mean age of the study population was 31.5 years with an age range of 18 to 56. 86 were female and 14 were male and the duration of headaches ranged from 4 months to 40 years. Diagnoses were based on the International Classification of Headache Disorders -2nd edition criteria. 41 patients experienced chronic migraine without aura, 45 migraine without aura, and 14 migraine with aura, (1 with hemiplegic migraine and 1 with brainstem symptoms). The brain MRI was normal in 81 patients including the patients with hemiplegic migraine and migraine with brainstem symptoms. White matter foci of hyperintense FLAIR were noted in 13 patients. 2 patients had a Chiari 1 malformation of 3-4 mm without evidence of compression. 1 patient had trace sinusitis with trace sphenoid fluid, 1 with a small arachnoid cyst and 1 with a venous angioma. A meningioma was detected in a patient with a 20 year history of bifrontal headaches occurring 20 - 30 days/month consistent with chronic migraine without aura. There had been no change in the character or pattern of the headaches and the patient did not report neurologic symptoms (Table 1).

We used data from the analysis by Katzman et. al. that examined the Incidental Findings on Brain MRI from 1000 Asymptomatic Volunteers and found that 4 subjects had brain tumors, 2 benign, 1

low grade glioma and 1 low grade oligodendroglioma[8]. We then utilized the data from the study by Vernooij et. al. that looked at Incidental Findings on Brain MRI in the General Population and found 31 benign tumors out of 2000 subjects[9]. Combining the cohorts there were 35 out of 3000 subjects with benign brain tumors. Fisher's exact was used to compare the proportion between the two cohorts (1 out of 100 in our study population and 35 out of 3000 in the two combined cohorts). The calculated p-value is > 0.99 indicating that there is no statistical difference between these rates.

Thus the one tumor detected in our study group was an incidental abnormal finding with a prevalence that would be expected in the general asymptomatic population.

DISCUSSION

The purpose of this study was to determine if patients had more insight with regard to detecting a potentially serious occult structural abnormality as the cause of their headaches than the examining neurologist. All of the patients in this study met the International Classification of Headache Disorders 2nd edition criteria for migraine and had a normal neurologic exam[9]. There were no "red flags" such as change in character and pattern, new neurologic symptoms, cough/exertional headache or an underlying

medical illness and the treating neurology clinician did not think that imaging of the brain was indicated.

82 scans were completely normal which was identical to the percentage that was found in the study by Katzman et al[8]. 13 scans revealed deep white matter hyperintensities which are a common finding in migraine and likely of no clinical significance[4,5]. There was one arachnoid cyst with an expected prevalence of 1.1 % in the general asymptomatic population[8]. One developmental venous anomaly was detected and they are found in up to 3 % of asymptomatic patients and almost always have a benign course[10]. Asymptomatic Chiari 1 malformation with the cerebellar tonsils extending more than 5 mm below the foramen magnum has a prevalence of approximately 1 % in the general population and accompanying syringomyelia is rare[11]. In our study 2 patients had a Chiari 1 malformation of less than 5 mm, without evidence of compression and of no clinical significance. Asymptomatic sinus disease is another extremely common incidental MRI finding and was present in 1 patient.

The one significant finding in our cohort was a meningioma in a patient with a 20 year history of headaches occurring 20 to 30 days/month with one severe episode always in association with menses consistent with chronic migraine without aura. The brain MRI revealed a 3.5 cm x 2.6 cm x 3.3 cm right posterior frontal convexity extra-axial mass with displacement of the adjacent brain parenchyma and moderate vasogenic edema. Surgical excision was performed and pathology revealed the lesion to be a grade 2 meningioma. The patient received postoperative radiation therapy. The headaches improved initially but rapidly returned to daily.

The argument will be made that the detection of one clinically significant abnormality justifies performing brain MRI on all patients with migraine, however based on the results of large studies that looked at incidental findings in the general population

that premise would require that a brain MRI be performed on everyone[8,9]. The prevalence of asymptomatic primary brain tumors in the general population identified on brain MRI is approximately 1% and about 25% are meningiomas[8,9,12]. Furthermore in the study of brain MRI in 1000 asymptomatic volunteers 1.1% required an urgent referral which is almost identical to what was required in our cohort[8]. Performing an MRI on everyone is not feasible and our study demonstrates that there is no indication for a brain MRI in patients with a diagnosis of migraine and a normal neurologic exam. Furthermore it does not appear that patients have any more insight than the treating clinician in diagnosing an unsuspected structural abnormality.

More than 1 billion dollars are spent each year on unnecessary brain imaging in the evaluation of primary headache disorders[13]. Performing brain imaging without a clear clinical indication solely at the insistence of the patient should be avoided.

CONCLUSION

Headache is an extremely common symptom that is usually indicative of a benign headache syndrome. Despite that fact many patients will undergo unnecessary cranial imaging simply to allay their fear of an underlying structural cause.

This study showed that patients who present for evaluation of headaches that are consistent with migraine and have a normal neurologic exam do not possess unaccountable intuition regarding detection of an occult brain abnormality. Brain MRI in the evaluation of headache should only be performed when there is reasonable clinical suspicion of underlying structural disease and not solely at the insistence of the patient and this should constitute the standard of care.

We wish to thank Dr. Wei Wang from the Brigham and Women's Hospital and Harvard Medical School for her assistance *with the* statistics *used in this paper.*

The statistical work was conducted with support from Harvard Catalyst, The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award UL1 TR001102) and financial contributions from Harvard University and its affiliated academic healthcare centers. The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic healthcare centers, or the National Institutes of Health.

REFERENCES

1) Smitherman TA, Burch R, Sheikh H, Loder E. The prevalence, impact, and treatment of migraine and severe headache in the United States: a review of statistics from

national surveillance studies. Headache. 2013. 53(3): 427-436.

2) Sempere AP, Porta-Etessam J, Medrano V et al. Neuroimaging in the evaluation of patients with non-acute headache. Cephalalgia 2005; 25:30-35

3) Bashir A, Lipton RB, Ashina S, Ashina M. Migraine and structural changes in the brain: A systematic review and meta-analysis. Neurology. 2013;81:1260-1268.

4) Swartz RH, Kern RZ. Migraine is associated with magnetic resonance imaging white matter abnormalities: a meta-analysis. Arch Neurol 2004: 61:1366-1368.

5) Palm-Meinders IH, Koppen H, Terwindt GM et al. Structural Brain Changes in Migraine Structural Brain Changes in Migraine. *JAMA* 2012; 308:1889-1897

6) Osborn RE, Alder DC, Mitchell CS. MR Imaging of the Brain in Patients with Migraine Headaches. AJNR; 12:521-524.

7) Headache Classification Subcommittee of the International Headache Society . "The International Classification of Headache Disorders, 2nd Edition" . Cephalagia 2004. 24(1); 8-160.

8) Katzman GL, Dagher AP, Patronas NJ. Incidental Findings on Brain Magnetic Resonance Imaging From 1000 Asymptomatic Volunteers. JAMA 1999; 282:36-39.

9) Vernooij MW, Ikram MA, Tanghe HL, et al. Incidental findings on brain MRI in the general population. NEngl J Med. 2007; 357:1821-1828.

10) Mooney MA, Zabramski JM. Developmental venous anomalies. Handbook of Clinical Neurology 2017; 143:279-282.

11) Meadows J. Kraut M, Guarnieri M, Haroun RI, Carson BS. Asymptomatic Chiari Type 1 malformation identified on magnetic resonance imaging. J Neurosurg. 2000;92:920-926.

12) Is the incidence of meningiomas underestimated? A regional survey. BJ Cancer 2008; 99:182-184.

13) Callaghan BC, Kerber KA, Pace RJ, Skolarus LE, Burke JF. Headaches and Neuroimaging. JAMA Internal Medicine, 2014; 174(5): 819-821.

TABLE 1. MRI Findings

Female-84 Male–14 **Age – 18-56** **Duration of headaches - 4 months to 40 years**
Migraine without aura- 41 **Migraine with aura- 14 (1 with hemiplegic migraine, 1 with brainstem symptoms, 1 with trace sphenoid fluid- CT sinuses negative)** **Chronic migraine- 45** **Brain MRI**
Normal- 82 **Foci of hyperintense FLAIR- 13** **Chiari malformation- 2 (3-4 mm below the foramen magnum both with migraine without aura)** **Arachnoid cyst- 1 (migraine without aura)** **Venous angioma- 1 (migraine without aura)** **Mmeningioma with compression of the cortex and vasogenic edema- 1 (chronic migraine)**