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Significant and nonsignificant findings on magnetic resonance imaging of patients with headache

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ABSTRACT

Aim: The great majority of people suffer from headaches. Neuroimaging has a very limited role in determining the etiology of headache However, neuroimaging, especially magnetic resonance imaging (MRI), is requested for the vast majority of patients with headache. We aimed to determine the frequency of clinically significant and nonsignificant findings on brain MRI in patients with headache, and the factors associated with these findings.

Material and Method: A total of 350 patients (231 women and 119 men), who underwent MRI examinations for headache complaints, were included in the study. Based on the evaluation of lesions detected on MRI and headache characteristics together, lesions associated with headache were classified as significant findings, and lesions unrelated to headache were classified as nonsignificant findings. Patients were compared in terms of brain MRI findings on the basis of age, gender, and duration of headache complaints.

Results: Assessment of brain MRIs revealed normal findings in 211 (60.3%) patients, nonsignificant findings in 122 (34.8%) patients, and significant findings that could cause headache in 17 (4.9%) patients. The most common significant lesions were acute sinusitis, acute cerebrovascular accident, cerebral venous sinus thrombosis and aneurysm. In patients over 65 years of age, the frequency of significant findings was significantly higher (p:0.001). The frequency of significant findings was higher in male patients and patients with a headache duration of less than one month, but there was no statistical difference (p:0.452 and p:0477).

Conclusion: We found significant findings on brain MRI in approximately 5% of patients with headache. Being over 65 years old and acute onset headache increase the probability of detecting significant lesions on MRI. Despite its low diagnostic value, physicians will often refer patients with headaches to neuroimaging for fear of missing a critical underlying lesion and encountering medico-legal issues. Taking into account worrying red flags can increase the likelihood of finding significant lesions.

Keywords: Headache, neuroimaging, magnetic resonance imaging

INTRODUCTION

Headache is one of the most common complaints in population. Its lifetime prevalence is over 90% (1). All health care providers, especially neurologists, frequently encounter the problem of headache. According to the International Headache Society classification, headaches are divided into two basic groups: primary and secondary. There is no underlying detectable cause of primary headaches. The most common primary headache types are tension-type headache and migraine. In secondary headaches, headaches appear as a symptom depending on an underlying cause such as infection, metabolic disorder, vascular diseases, trauma, and brain tumors (2,3).

Today, as in the past, the history and physical examination findings play a significant role in the differential diagnosis of headache. However, with rapid technological advancements, numerous diagnostic methods, particularly brain magnetic resonance imaging (MRI), have become widely used in the differential diagnosis of headache. Brain MRI findings are usually normal in the vast majority of patients with headache (4,5). However, nowadays, physicians frequently utilize neuroimaging techniques to exclude life-threatening secondary causes of headaches. Other reasons for the frequent use of neuroimaging methods are patient requests and medico-legal concerns (5–8).

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The excessive usage of neuroimaging, particularly MRI, has increased the likelihood of incidental lesion detection (7,9,10). The detected incidental lesions can sometimes entangle the diagnosis process rather than contributing in the accurate diagnosis. Sometimes, headache is attributed to these incidental lesions, and detailed evaluation of the patients' mental, hemodynamic and metabolic conditions is ignored (9). Therefore, the diagnosis of the actual problems underlying the headache may be delayed.

Some studies have brought attention to certain important red flags that predict the possibility of detecting a significant lesion on MRI in patients with headache (3,11). Therefore, it has been proposed that applying neuroimaging in selected cases under the guidance of these red flags will contribute to a cost-effective process as well as help early diagnosis (3,5,7,12,13).

In this study, we aimed to determine the frequency of clinically significant and nonsignificant findings on brain MRI in patients with headache and investigate the relationship of these findings with the characteristics of headache and demographic data of the patients.

MATERIAL AND METHOD

This retrospective study was approved by Ankara City Hospital No: 1 Clinical Research Ethics Committee (Date: 2022, Decision No: E1/2295/2022). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients who presented to our neurology outpatient clinic in September 2019 and October 2019 with complaints of headache were analyzed retrospectively. Patients with a history of primary headache and known intracranial neoplasia were not included in the study. Patients who had recently had a head injury were also excluded from the study. A total of 350 patients, 231 (66%) women and 119 (34%) men, who underwent MRI examinations for headache complaints, were included in the study.

The patients' age, gender, smoking habits, comorbid diseases, and headache duration were all recorded. If patients have other complaints accompanying headache and abnormal neurological examination findings, this information was recorded.

Two expert neurologists reviewed the brain MRI scans and reports. The detected lesions and the headache characteristics of the patients were compared:

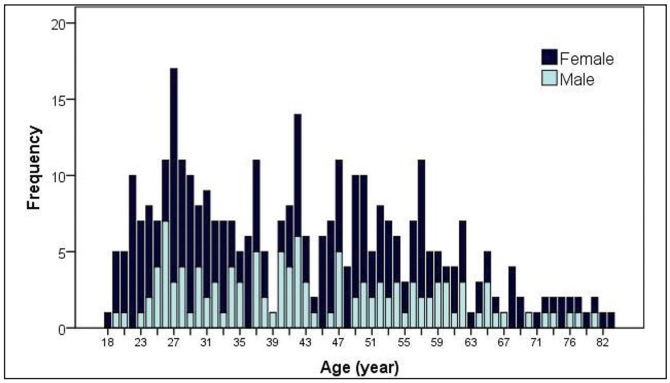
- Lesions corresponding to the headache characteristics were accepted as “significant lesions”.
- Lesions that did not correspond with the headache characteristics were accepted as "nonsignificant (incidental) lesions".

The patients were divided into three different groups according to the duration of the headache (less than one month and one month or more), age (under 65 years old and over 65 years old), and gender. Based on these groupings, patients were compared in terms of brain MRI findings.

All statistical analyses were done using IBM SPSS statistic 22.0 (Chicago, IL, USA). Numerical variables were expressed as mean±SD. Comparisons of numerical variables were made using Student's t-test. Categorical variables were compared using the Chi-Square test. A $p<0.05$ level was considered statistically significant.

RESULTS

The mean age was 42.63±15.06 years (**Graphic 1**). The study group consisted of 231 (66%) female and 119 (34%) male patients. The mean duration of headache complaint was 23.37±27.27 months. The two most common comorbid diseases detected in our patients were hypertension (80 patients, 22.9%) and psychiatric disorders (68 patients, 19.4%). Other common comorbid diseases are shown in **Table 1**.



Graphic 1. Age and gender distribution of patients with headache

Assessment of brain MRIs revealed normal findings in 211 (60.3%) patients, insignificant findings in 122 (34.8%) patients, and significant findings that could cause headache in 17 (4.9%) patients. The most common significant finding in the patients was sinusitis (5 patients, 1.4%). One of the patients with acute cerebrovascular accident (CVA) presented with only headache, and the neurological examination was normal. However, MRI showed multiple sub-acute millimetric infarcts. In the other acute CVA patient who presented with headache and tinnitus, no significant abnormal finding was detected in the neurological examination. MRI demonstrated acute 4 millimeters (mm) left cerebellar infarction. One of the two patients with acute cerebral venous sinus thrombosis presented with headache only, while the other had eyelid twitching and headache complaints. There were no significant

abnormal findings in the neurological and funduscopic examinations of both. The patient with pseudotumor cerebri had a complaint of headache and decreased vision in the left eye. Fundoscopic examination revealed papilledema on the left side. MRI of the patient with pseudotumor cerebri demonstrated that the height of the pituitary gland decreased according to the patient's age, slight enlargement of the suprasellar cisterna, and prominent subarachnoid space around the optic nerves.

The three most common nonsignificant findings in our study group were white matter hyperintensity (52 patients, 14.9%), paranasal sinus problems (26 patients, 7.4%), and arachnoid cysts (13 patients, 3.7%). In three patients with meningioma, the lesions were smaller than 5 mm and did not have a critical localization. Parietal capillary telangiectasia was found in one of the two patients with vascular malformation, and a frontal hemangioma smaller than 5 mm was found in the other. In two patients with Chiari malformation, downward displacement was shorter than 3 mm. We detected choroid plexus lesions in three of our patients. One of our patients had mild contrast enhancement in the choroid plexus, the other had a small papilloma, and the last one had small xanthogranulomas in lateral ventricles. These lesions were insufficient to explain the headache complaints of our patients. We detected partial empty sella in two of our patients. None of them were associated with pseudotumor cerebri.

All of the rare significant and nonsignificant findings are presented in **Table 1**.

During the investigation of the etiology of headache, 13 (3.7%) patients were diagnosed with hypertension. In 11 of the newly diagnosed hypertension cases, the duration of the headache complaint was less than 12 months. No significant finding was detected in MRI in any of these cases.

Psychiatric comorbidity was detected in 68 patients, including anxiety in 43 patients, depression in 20 patients, obsessive-compulsive disorder in 3 patients, and psychotic disorder in 2 patients. Only one (1.5%) of these cases had a significant finding (pituitary macroadenoma) on brain MRI.

Thirty-one (%8.9) of our patients were aged 65 and over. When we grouped our patients as <65 years and ≥65 years of age, the difference between the groups in terms of brain MRI findings was statistically significant (p:0.001). While 63.6% of patients under 65 years of age had normal brain MRI findings, only 22.6% of patients 65-year-old or older had normal brain MRI findings. Both significant (12.9%) and nonsignificant (64.5%) brain MRI findings were found to be significantly more common in the 65-year-old or older group (**Table 2**).

Table 1. Demographic and clinical data of the study group

	All Cases (n:350)
Age (year)	42.63±15.06
Gender Female/Male	231 (66%)/119 (34%)
Smoking	44 (12.6%)
Duration of headache complaint (month)	23.37±27.27
Comorbidities	
Coronary artery disease	21 (6.0%)
Hypertension	80 (22.9%)
Hyperlipidemia	19 (5.4%)
Diabetes mellitus	29 (8.3%)
Neurological diseases	17 (4.9%)
Psychiatric diseases	68 (19.4%)
Anxiety	*43 (12.2%)*
Depression	*20 (5.7%)*
Obsessive-compulsive disorder	*3 (0.9%)*
Psychotic disorder	*2 (0.6%)*
Newly diagosed hypertension cases	13 (3.7%)
Brain magnetic resonance imaging findings	
Normal	***211 (60.3%)***
Nonsignificant findings	***122 (34.8%)***
White matter hyperintensity	52 (14.9%)
Paranasal sinus diseases	26 (7.4%)
Arachnoid cyst	13 (3.7%)
Atrophy	10 (2.9%)
Cerebral-cerebellar atrophy	*4 (1.2%)*
Cerebral atrophy	*5 (1.4%)*
Focal atrophy	*1 (0.3%)*
Encephalomalasic changes	5 (1.4%)
Meningioma	3 (0.9%)
Choroid plexus lesion	3 (0.9%)
Chiari malformation	2 (0.6%)
Empty sella	2 (0.6%)
Pineal cyst	2 (0.6%)
Vascular malformations	2 (0.6%)
Neuroglial Cyst	1 (0.3%)
Colpocephaly	1 (0.3%)
Significant findings	***17 (4.9%)***
Sinusitis	5 (1.4%)
Acute cerebrovascular accident	2 (0.6%)
Acute cerebral venous sinus thrombosis	2 (0.6%)
Aneurysm	2 (0.6%)
Otitis media	2 (0.6%)
Triventricular hydrocephalus	1 (0.3%)
Pituitary macroadenoma	1 (0.3%)
Cavernous hemangioma	1 (0.3%)
Pseudotumor cerebri	1 (0.3%)

Table 2. Comparison of patients' MRI findings grouped by age, duration of headache and gender

	Normal findings n: 210	Nonsignificant findings n: 123	Significant findings n: 17	p
Age (year)				0.001
< 65	203 (63.6%)	103 (32.3%)	13 (4.1%)	
≥ 65	7 (22.6%)	20 (64.5%)	4 (12.9%)	
Duration of headache complaint				0.477
< 1 month	49 (55.7%)	33 (37.5%)	6 (6.8%)	
≥ 1 month	161 (61.5%)	90 (34.4%)	11 (4.2%)	
Gender				0.452
Female	142 (61.5%)	80 (34.6%)	9 (3.9%)	
Male	68 (57.1%)	43 (36.1%)	8 (6.7%)	

When the patients were grouped as those with headache less than one month (88 patients, 25.1%) and those with one month or longer (262 patients, 74.9%), no significant difference was found between the groups in terms of brain MRI findings (p:0.477). Although it was not statistically significant, the frequency of significant findings was higher in patients with headache less than one month old (6.8%) (**Table 2**).

When the patients were compared by gender, significant brain MRI findings were observed more frequently in male patients (6.7%) than in female patients (3.9%), but there was no statistical difference (p:0.452) (**Table 2**).

DISCUSSION

We found significant lesions associated with headache on brain MRI of approximately 5% of patients. On MRI of approximately one-third of the patients, we detected incidental lesions unrelated to the described headache characteristics. The incidence of significant lesions on brain MRI was significantly higher in elderly patients. The most common comorbid diseases in patients presenting with headaches were hypertension and psychiatric diseases. The frequency of significant lesions associated with headache on brain MRI was rare in patients with psychiatric comorbidities. Newly diagnosed hypertension was common in patients with headache complaint duration of less than one year.

Headache is among the most common complaints in both men and women. The majority of headaches are primary headaches. Secondary headaches caused by underlying pathologies such as vessels, nerves, and other structures in the head and neck region, and systemic diseases are less common than primary headaches (1,3). While neurological examination findings and neuroimaging findings are generally normal in primary headaches, significant pathological lesions can be seen on neuroimaging in a small portion of secondary headaches. Therefore, people suffering from headaches should be carefully and extensively investigated (3,11).

In the evaluation of headaches, careful patient history and detailed neurological examination are the most critical steps. Theoretically, in the light of the information obtained from the history and neurological examination, it should be decided whether a further examination is needed (3,9,13). However, a significant portion of patients with headache complaints are directed to neuroimaging in daily hospital practices (9). In studies, neuroimaging has detected significant lesions in a very small proportion of patients with headaches. The frequency of finding significant lesions on neuroimaging has been reported between 0.18% and 2.1%.(7,14) However, in our study, we found significant findings that could explain the headache on brain MRI in only 4.9% of our patients. The frequency of detecting significant lesions in our study was slightly higher than in other studies. One of the reasons for this situation may be that we did not include patients with a previous primary headache diagnosis in our study because neurological imaging findings are mostly normal in these patients. Another reason may be that we accept the signs of acute sinusitis as a significant lesion.

Neuroimaging helps to diagnose very few patients during the evaluation of headaches. Thus the reasons for its overuse are still open to debate. Today, neuroimaging tests are preferred as an exclusion tool for serious underlying pathologies rather than a diagnostic test when investigating the etiology of headaches (1,5,7). The physician's fear of missing a significant lesion that may cause headaches is an important reason for the frequent use of neuroimaging. Another reason is the concerns of the patients and their relatives over the ongoing headache. Increasing medico-legal problems in recent years is another important reason. Under the pressure of patient worry on the one hand and medico-legal reasons on the other, the physician tends to use neuroimaging despite the absence of any medical indications (12,15–17).

In recent years, significant advances have been made in neuroimaging devices, including MRI. Advances in imaging techniques allow good characterization of detected lesions. However, advances in imaging technology have often led to detecting clinically nonsignificant incidental lesions and anatomical variants (10). Under the influence of the same medico-legal concerns, radiologists started to report these clinically nonsignificant incidental lesions in detail. As a result, insignificant incidental lesions, which may even be multiple, on brain MRI reports have increased rather than reduced both the clinician's and the patient's concerns. Furthermore, sometimes these incidental lesions and detailed defensive reports lead the physician to refer to invasive procedures such as lumbar puncture and angiography in the differential diagnosis of headaches (7,8,15). These invasive procedures cause an increased medical and economic burden as well as significant problems such as increased complication occurrence. The incidence of incidental lesions in patients with headaches has been reported between 4.3% and 46% (10,14). In our study, we found incidental lesions unrelated to their headache in 35.1% of patients on brain MRI. Consistent with the literature, most of the incidental lesions in our patients consisted of benign changes that occur with aging, such as white matter hyperintensities and atrophy and some structural changes.

Some authors have drawn attention to various red flags that suggest significant lesions that may cause headaches in patients. They emphasized the increase in the probability

of identifying significant findings on brain MRI in the presence of these red flags. It has been proposed that headaches, which start at advanced ages, may sometimes occur secondary to serious diseases (11,13,15). We found a high rate (12.9%) of significant findings on brain MRI in our patients aged 65 years and older with headaches. Acute headache has also been considered as a predictor of significant lesions. The chance of detecting significant findings on MRI in acute-onset headaches can reach 20%, especially in selected cases (12). We found the frequency of significant findings slightly higher in cases with headache onset less than one month compared to other patients. In a previous study, the female gender was found to be a risk factor for significant MRI findings (12). However, in some other studies, significant findings on neuroimaging were found more frequently in male patients (8,15). In our study, the frequency of significant findings on brain MRI was higher in male patients than in female patients, but the difference was insignificant. In addition, changes in headache character, gradual increase in pain intensity and presence of other symptoms accompanying headache are risk factors for detecting significant findings in MRI (12–14). Budweg et al. (12) showed that approximately half of the patients with significant findings on brain MRI had positive neurological examination findings.

Comorbid diseases such as hypertension, metabolic, cardiovascular, neurological, and psychiatric diseases are frequently observed in patients with headaches (18). Akyıldız et al. (19) reported the prevalence of psychiatric disease in patients with headaches at a very high rate of 80%. Psychiatric disorders were the second most common comorbid disease in our study population. We found less frequent significant findings on brain MRIs of patients with psychiatric comorbidities. The relationships between psychiatric diseases and headaches are complex and multifaceted. Psychiatric diseases have a negative effect on headache management (18,20). Therefore, the evaluation of headache patients with psychiatric comorbidity together with a psychiatrist may affect the rate of need for MRI in the differential diagnosis of these patients.

In our study, the most common comorbid disease accompanying headache was hypertension. In addition, we found a high frequency of newly diagnosed hypertension among patients with a headache complaint of less than a year. Providing effective blood pressure control in these patients may reduce headache complaints, and as a result, unnecessary MRI can be avoided. On the other hand, close monitoring of blood pressure before starting further investigations in middle-aged patients with headaches may enable us to detect new-onset hypertension cases that are overlooked and may reduce the need for further investigations.

CONCLUSION

We found significant findings on brain MRI of 5% of patients with headaches. Being over 65 years old and acute onset headache increase the probability of detecting significant lesions on MRI. When neuroimaging is requested in the differential diagnosis of patients presenting with headaches, informing patients about possible nonsignificant incidental lesions will reduce the concerns of patients and their relatives. Although its diagnostic ability is low, physicians will continue to use neuroimaging frequently in patients with headaches to avoid missing a critical underlying lesion and not be entangled with medico-legal problems. However, considering alarming red flags may increase the probability of finding significant lesions.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by Ankara City Hospital No: 1 Clinical Research Ethics Committee (Date: 2022, Decision No: E1/2295/2022).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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