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Brain MRI findings in patients with Idiopathic Hypersomnia

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Abstract

Objective—Proper diagnosis of idiopathic hypersomnia necessitates the exclusion of neurologic or medical causes of sleepiness that better explain the clinical syndrome. However, there are no formal guidelines regarding the use of neuroimaging to identify such secondary causes of symptoms. We sought to characterize brain MRI findings in a series of patients with idiopathic hypersomnia.

Methods—We reviewed medical records on a consecutive series of 61 patients diagnosed with idiopathic hypersomnia to determine the frequency and results of brain magnetic resonance imaging (MRI).

Results—One-third of patients had undergone brain MRI, with focal neurologic signs or symptoms being the most common indication for neuroimaging. Although seven patients had an identifiable finding on neuroimaging (e.g., chronic microvascular ischemic changes), clinical management was changed as a result of imaging in only three cases. In all three, the imaging finding was predated by clear clinical abnormalities.

Conclusions—Neuroimaging may be a complementary part of an idiopathic hypersomnia evaluation, but the decision to pursue imaging should be made on a case-by-case basis.

Keywords

hypersomnolence; idiopathic hypersomnia; magnetic resonance imaging; neuroimaging; sleep disorders; narcolepsy

1. INTRODUCTION

Idiopathic hypersomnia is a central nervous system hypersomnolence disorder that manifests as pathologic daytime sleepiness despite sufficient sleep at night. Hypersomnia is associated with higher healthcare costs and significant socioeconomic burdens for affected patients [1]. Formal diagnostic criteria for idiopathic hypersomnia, through the International

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Classification of Sleep Disorders, require the presence of sleepiness lasting at least three months, accompanied by the demonstration of short sleep latency, without abnormal REM sleep, on multiple sleep latency test or the documentation of persistently long sleep times by actigraphy or polysomnography [2]. These diagnostic criteria also explicitly require the exclusion of other medical conditions that could account for hypersomnolence. However, there are no formal recommendations on when brain imaging should be performed as part of the work up to exclude structural neurologic conditions.

Narcolepsy types 1 and 2 are two other central hypersomnolence disorders that share some features with idiopathic hypersomnia, notably the pathologic degree of daytime sleepiness. These disorders have been shown in some cases to be “secondary”, i.e., caused by an identifiable structural brain lesion, frequently involving the hypothalamus. Such secondary, structural causes of narcolepsy include neurosarcoidosis [3], craniopharyngioma [4, 5], neuromyelitis optica spectrum disorders [6–10], and anti-Ma-2 encephalitis [11]. Kleine-Levin syndrome, an episodic form of central nervous system hypersomnolence, has also recently been demonstrated to occur following surgical resection of a colloid cyst [12]. Given these cases of structural lesions resulting in pathologic sleepiness, we sought to evaluate the frequency and results of neuroimaging in a cohort of patients with idiopathic hypersomnia.

2. MATERIALS AND METHODS

We performed a retrospective chart review of 61 consecutive patients meeting International Classification of Sleep Disorders, third edition, diagnostic criteria for idiopathic hypersomnia. All patients were evaluated in our sleep clinic by a board-certified sleep medicine specialist and had undergone nocturnal polysomnography (PSG) and multiple sleep latency testing (MSLT) for suspicion of a central disorder of hypersomnolence (i.e., idiopathic hypersomnia or narcolepsy type 1 or 2). Cases were reviewed to determine which patients had undergone MRI of the brain, results of imaging, and features of idiopathic hypersomnia symptomatology. Hypersomnolence characteristics collected included: age at symptom onset, age at evaluation, average estimated weekly sleep time (per patient report), presence or absence of problematic sleep inertia, number of medications attempted for treatment of hypersomnolence, and PSG/MSLT features. Clinical characteristics of those who did and did not undergo imaging, and those who had abnormal and normal results, were compared using t-tests (corrected for unequal variance when appropriate) or Fisher exact test. This chart review was approved by our local Institutional Review Board.

3. RESULTS

Of 61 patients, 22 (36%) had undergone MRI of the brain and results were available for review in 21. Results from the remaining one patient could not be obtained and the subject was excluded from further analyses. There was a higher proportion of women in the group without imaging (97% versus 76%, $p = 0.02$), but otherwise there were no significant demographic or clinical differences between those with and without MRI testing. The group of imaged patients consisted of 16 women and 5 men, with a mean age of 38.0 years (SD = 11.7). The diagnosis of idiopathic hypersomnia was confirmed via mean MSLT sleep latency

of less than 8 minutes (mean 4.2, SD 2.0) with fewer than two sleep onset REM periods (mean 0.2, SD 0.4). Sleep apnea was not present (mean apnea-hypopnea index 1.2, SD 1.1). Indications for performing MRI were: focal neurologic signs or symptoms (n = 5, 24%), headache (n = 3, 14%), memory loss or cognitive dysfunction out of proportion to that expected from hypersomnolence (n =3, 14%), spells (n = 2, 10%), and one each (5%) of abnormal cerebrospinal fluid protein level, focal slowing on EEG, galactorrhea, and low serum cortisol level. Hypersomnolence itself was the sole indication for imaging in 4 patients (19%). In 12 cases, MRI was performed before the initial assessment for idiopathic hypersomnia at our center, having been ordered by the patients' prior sleep physician in only 2 cases. Of the remaining 9 patients with MRIs, the imaging was ordered by the authors in 6 cases and by non-sleep physicians in 3 cases, after our initial evaluation.

MRIs were read as normal in 67% of patients (n = 14). Clinical features were similar between those with normal and abnormal MRI results, although those with abnormal neuroimaging results were younger and had fewer periodic limb movements of sleep (Table 1). Among the 7 cases with abnormal imaging, mild chronic microvascular ischemic changes were seen in 2 patients. No other imaging abnormality was noted in more than one patient. These other abnormalities included incidental cyst, Chiari I malformation, evidence of increased intracranial pressure without a mass (i.e., idiopathic intracranial hypertension), pituitary adenoma, and pituitary enhancement thought likely to represent normal heterogeneity versus microadenoma. Clinical management was changed as a result of imaging in 3 of these patients. The patient with Chiari I malformation underwent surgical decompression for focal neurologic symptoms attributable to the Chiari malformation. Post-operatively, his neurologic symptoms were improved and family reported increased alertness, but he declined to return for sleep reassessment. The patient with signs of increased intracranial pressure was followed serially by neuro-ophthalmology for mild idiopathic intracranial hypertension, while her sleepiness persisted. The patient with a pituitary adenoma underwent trans-sphenoidal resection of his adenoma without impact on his longstanding subjective sleepiness; his MSLT establishing the diagnosis of idiopathic hypersomnia was performed several months subsequent to his surgery. In all three of these cases where MRI results prompted a change in management, focal neurologic signs or specific endocrine symptoms (i.e., galactorrhea) were the indication for MRI, rather than solely hypersomnolence.

4. DISCUSSION AND CONCLUSIONS

In this series of 60 patients with idiopathic hypersomnia, imaging was performed in one-third of patients, and abnormal neuroimaging findings were present in one-third of this subgroup. However, identified findings were often non-specific or incidental. Clinical management changed as a result of an MRI abnormality in three cases. This was a retrospective case series of patients seen in a sleep medicine clinic, and as such may have inadvertently excluded patients who were evaluated by other specialists (e.g., general neurologists) for their hypersomnolence and were found to have a causal structural lesion. A prospective series with a broader clinical catchment area would be helpful in capturing these additional subjects. The patients included in this series may have had atypically severe or medication-refractory idiopathic hypersomnia, because they were seen at a tertiary-referral

center, as suggested by the average of 4.5 medications for hypersomnolence tried by patients.

Comparisons between groups on features of idiopathic hypersomnia symptoms and sleep testing results should be considered exploratory, but several group differences were noted. First, a much higher proportion of men with idiopathic hypersomnia underwent brain MRI than did women (83% versus 30%). This suggests that a bias might exist toward imaging men who report idiopathic hypersomnia symptoms, despite there being no difference in the likelihood of an abnormal MRI finding by gender in this study. Second, patients with abnormal imaging findings tended to have fewer periodic limb movements of sleep. However, in both groups, the average number of periodic limb movements was below the clinical threshold of 15 movements per hour, suggesting this difference may not be of clinical significance.

In our series, all patients with abnormal imaging findings that necessitated a change in clinical management had abnormal clinical findings prior to imaging, in addition to having symptoms of hypersomnolence. This suggests that brain MRI testing might not be needed in all patients with idiopathic hypersomnia to rule out secondary causes of hypersomnolence, but rather that the need for imaging should be individualized, taking into account the presence or absence of other signs and symptoms. However, this should be confirmed in a larger, prospective series. Pending such investigations, our practice is to perform imaging in patients in patients with localizing neurologic signs or symptoms and to consider performing imaging in those patients who are refractory to standard treatments for idiopathic hypersomnia, have atypical features of IH, or both. Alternate neuroimaging techniques such as diffusion tensor imaging and functional MRI have shown promise in other hypersomnolence disorders [13–15] and may prove similarly valuable in idiopathic hypersomnia. This remains an incompletely understood disorder, but one that ultimately might be definable by markers other than routine structural neuroimaging [16].

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Highlights

1. Idiopathic hypersomnia diagnosis requires exclusion of focal lesions.
2. Among 60 well-characterized IH patients, 1/3rd received brain MRI imaging.
3. Seven IH patients had a structural abnormality on MRI.
4. These findings did not clearly account for hypersomnia symptoms.

Table 1

Clinical characteristics of those with and without abnormal brain MRI imaging

	Normal Brain MRI (n = 14)	**Abnormal Brain MRI[1] (n = 7)**	**p–value[2]**
Current age, in years	**41.7 (9.3)**	**30.6 (13.1)**	**0.04**
Age of sleepiness onset	26.1 (17.3)	19.9 (4.7)	0.22
Female gender	12 (86%)	4 (57%)	0.72
Weekly sleep duration	68.7 (22.0)	73.2 (17.5)	0.64
Total sleep time in min (on PSG)	385.5 (38.4)	402.0 (53.7)	0.43
Percent sleep efficiency (on PSG)	90.4 (5.9)	89.5 (6.9)	0.77
Apnea-hypopnea index (on PSG)	1.0 (0.8)	1.5 (1.5)	0.47
Periodic limb movement index (on PSG)	**9.2 (9.8)**	**2.3 (2.9)**	**0.04**
Mean sleep latency in minutes (on MSLT)	4.1 (2.2)	4.4 (1.5)	0.74
One sleep-onset REM period present (on MSLT)	2 (14.3%)	2 (28.6%)	0.59

Values are mean (standard deviation) for continuous variables and count (percentage) for categorical variables.

[1] Brain MRI abnormalities included: mild chronic microvascular ischemic changes, incidental hippocampal cyst, Chiari I malformation, evidence of increased intracranial pressure without a mass (i.e., idiopathic intracranial hypertension), pituitary adenoma, and non-specific pituitary enhancement.

[2] p-value reflects t-test or Fisher exact test, as appropriate. Abbreviations: PSG = nocturnal polysomnography; MSLT = multiple sleep latency test