White Matter Lesions in a Patient with Headache – Case Report and Review of the Literature

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Abstract

Magnetic resonance imaging has been widely used to aid the diagnostic process in patients with various disorders of the nervous system. White matter hyperintensities represent a frequent T2-MRI finding. They may be due to multiple sclerosis and other demyelinating diseases, systemic diseases and cerebrovascular disease, among other examples. Such lesions have also been described in patients with migraine. In this paper we present the case of a patient with unilateral headache attacks, accompanied by photophobia and phonophobia, whose MRI scan showed lesions of the cerebral white matter, reported as most likely due to multiple sclerosis. We review the literature on the topic and discuss some possible approaches to the differential diagnosis.

Keywords: Headache; Migraine; Multiple sclerosis; White matter hyperintensities

1. Introduction

Magnetic resonance imaging (MRI) has been widely used to aid the diagnostic process in patients with various disorders of the nervous system. Its application is becoming even more widespread nowadays, as more hospitals and medical centers have MRI facilities. As more patients are being referred for brain MRI scans, the number of incidental findings which are unlikely to be discovered using other imaging techniques such as computed tomography (CT) tends to increase. The presence of white matter hyperintensities (WMH) is a frequent T2-MRI finding (Bekiesinska-Figatowska, 2004). They correspond to lesions which cannot usually be seen on CT scans, and may be due to various disorders. These include multiple sclerosis (MS) and other demyelinating diseases, systemic diseases (systemic lupus erythematosus, Sjögren syndrome, etc.), and cerebrovascular disease, among other examples.
Even if the presence of WMH is not among the main characteristics of migraine, it has been described in the literature, and especially patients experiencing aura are known to be at increased risk for such lesions. While brain WMH are more prevalent in migraine patients than in the general population, the pathogenesis and the risk factors of these hyperintensities are not fully elucidated (Trauninger et al., 2011). Lesions can be non-specific and clinically insignificant in many cases, but sometimes the reason for their presence is an underlying disease. Most often the clinician's attention is directed towards MS, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS), or central nervous system vasculitis. Some vascular risk factors need to be evaluated in the specific patient as well, such as genetic prothrombotic factors and use of oral contraceptives, considering their possible causative role for MRI lesions (Gladstone and Dodick, 2005; Porter et al., 2005; Moschiano et al., 2007). A possible explanation of the nature of WMH in migraine, when not due to underlying disorders, could be that they represent the sequelae of microvascular ischemic changes during migraine attacks, as presumed by Aradi et al. (2012) according to the results of their quantitative 3.0-Tesla MRI study. Suggestive features were tissue damage with axonal loss, low glial cell density, and an enlarged extracellular space with an increased extracellular water fraction. WMH in migraine are generally not believed to contribute to disease progression or severity. The recently published results of a study by Palm-Meinders et al. (2012) demonstrated that 9 years after baseline women with migraine had a higher incidence of deep WMH while no association of migraine with progression of lesions was found in men. Nevertheless, the progression of lesions was not associated with an increased number or frequency of migraine headaches, neither with cognitive decline.

In the process of ruling out differential diagnoses in a patient with WMH, it is important to consider some characteristic radiological features. Lesions in migraine are usually multiple and small, located in the deep or periventricular white matter, best observed on T2-weighted or FLAIR sequences (Gladstone and Dodick, 2005). A study of Seneviratne et al. (2012) demonstrated predilective involvement of the frontal lobe in all subjects with WMH, while infratentorial hyperintensities were not seen in any of them. Similar results were reported by Kamson et al. (2012) who compared WMH in migraine and MS. The authors found that migraine WMH affected mainly the deep white matter and subcortical U-fibers, belonged to the anterior circulation, appeared more frequently in the frontal and parietal lobes, showed no difference in average size between lobes, and were smaller and fewer than in MS. Though some characteristic patterns were found for the two disorders, they were not considered reliable for accurate differential diagnosis of WMH in individual patients. The differential diagnosis between these conditions can be rendered even more difficult by the fact that not only WMH are seen in migraine, but headache and specifically migraine may be more frequent in MS patients than in the general population (Chipilski et al., 2001; Milanov, 2009). Headache may occur at onset and during the course of the disease, and can be exacerbated by disease-modifying therapies (La Mantia, 2009). It has been illustrated that isolated MS lesions in strategic regions like the midbrain may cause headaches similar to migraine (Putzki and Katsarava, 2010). Migraine may be comorbid with MS, but in addition it may be associated with a more symptomatic MS course (Kister et al., 2010). A hypothesis has been proposed, relating MS relapse-onset migraine headache to a possible dysregulation of the 5-HT system in the pathophysiology of MS (Sandyk and Awerbuch, 1994). In a comparative study including migraineurs and MS patients with and without migraine, Tortorella et al. (2006) found that MS patients with migraine had more lesions in the red nucleus, substantia nigra and
periaqueductal gray matter, thus suggesting a possible localization factor responsible for the presence of migraine in patients with MS. Brainstem and especially midbrain plaques in patients with MS could be associated with an increased likelihood of migraine headache as well (Gee et al., 2005). But while MS patients tend to have migraine or other types of headache as comorbidities, no distinctive "MS headache" can be described, and headache may not correlate with any clinical features of MS (Rolak and Brown, 1990). Similarities in symptoms between patients with migraine and MS presenting with headache can thus lead to misdiagnosis. MRI lesions which may be found in migraine patients with otherwise normal neurological examination may also cause significant patient anxiety (Elliott, 2007).

The fact that a large number of other disorders exist, which can present with a similar MRI picture, renders the differential diagnosis difficult in many cases. The diagnosis of multiple sclerosis tends to stand out when younger patients are sent for consultation to a neurologist or are admitted to a neurological clinic and present with a MRI scan showing multiple small white matter lesions. If the clinical criteria for multiple sclerosis are fulfilled, the MRI finding can be considered supportive of the diagnosis and the diagnostic process is generally straightforward. In other cases though, especially when there is neither clinical evidence, nor history data for any symptom or syndrome which can be attributed to multiple sclerosis, differential diagnoses should be discussed in depth.

2. Case report

We present the case of a 42-year-old male patient, K.S.T., who was referred to our clinic with complaints of relapsing headache, throbbing and pulsating in character, affecting the right half of the head, predominantly the parietal region. The headache had appeared about two months before the patient presented to the clinic. The attacks lasted from several hours to 1 day and were followed by remissions. During the periods of severe headache, the patient had photophobia and phonophobia, which were sometimes accompanied by hyperosmia. He tended to lie down and stay in a quiet and dark place until the alleviation of symptoms. No symptoms preceding the attacks were reported. Eletriptan was prescribed and had a good effect on controlling severe headache attacks. According to the patient, his mother used to have very similar complaints in her life.

After admission to the hospital the preliminary diagnosis of migraine was established, cluster headache and secondary headache being considered as the most important differential diagnoses. The patient fulfilled the criteria of IHS for migraine without aura (Headache Classification Subcommittee of the International Headache Society, 2004). Cluster headache was considered less likely, mostly because the time pattern was not typical and the patient did not report any autonomic signs, except for mild and inconsistent tearing.

Clinical examination was normal. Blood pressure was 120/80 mmHg. Neurological examination was normal. Laboratory assessment, including hematology, biochemistry and coagulation status was normal. MRI scan of the head and neck was performed in order to exclude headache secondary to a structural lesion. Twelve small, round, oval-shaped lesions were visualized in the white matter of the two cerebral hemispheres (Figs. 1 and 2). There were 4 subcortical lesions, 3 periventricular, 1 in the corpus callosum, and 3 in the centrum semiovale. They were hyperintense on T2 and T2-FLAIR images. One of the lesions appeared hypointense on T1. No lesions were seen in the infratentorial space. The lesions showed no contrast enhancement. The findings were described as
conforming to a demyelinating process, most probably multiple sclerosis. Cervical spondylosis and bulging discs at the C5-C6 and C6-C7 levels were found as well. EEG was performed showing irregular alpha rhythm but no paroxysmal activity. Visual evoked responses were normal. The patient was consulted by a neuroophthalmologist who described normal visual acuity for 100% and low contrast levels, and excavation of the optic discs on fundoscopy. Follow-up was suggested.

**Fig 1.** Axial T2-FLAIR brain MRI. Bilateral periventricular hyperintense lesions

**Fig 2.** Coronal T2-FLAIR brain MRI. Subcortical hyperintense lesions
3. Discussion

In this paper we present the case of a patient with unilateral headache attacks, accompanied by photophobia and phonophobia, whose MRI scan showed lesions of the cerebral white matter, reported by the radiologist as most likely due to multiple sclerosis.

When establishing the diagnosis we had several options, but two of them were considered better substantiated than the others. First, to accept that the patient has migraine, and to relate the white matter lesions to migraine, as it has been described by other authors. Though MRI findings were reported as compatible with MS, there were only supratentorial lesions, similar to those described in the literature in patients with migraine. The patient had a normal neurological examination, without any signs and symptoms suggestive of MS. Moreover, the clinical history showed no evidence of relapses or other neurological manifestations in the past. As MS remains above all a clinical diagnosis, and no clinical criteria were satisfied in our case, such diagnosis could not be established. The criteria for migraine without aura were fulfilled, another supportive detail being the good efficacy of eletriptan.

The differential diagnostic alternative we had was to admit that the patient had two probably independent diseases, migraine and multiple sclerosis, the latter presenting at this stage as a radiologically isolated syndrome. This could be plausible, assuming that the radiological findings in our case resemble to some extent those seen in MS. One should also bear in mind the extensive literature data about the clinico-radiological correlation and paradox in MS, especially in the initial stages of the disease. The comorbidity of MS and migraine found in a number of studies should be considered as well. Other theoretically acceptable diagnostic options, such as MS initially presenting with migraine-like headache, CADASIL, vasculitis, etc. were considered less likely, lacking enough supportive data in this specific case.

As there were not enough evidences for establishing the diagnosis of MS or of any other disorder among those most often discussed in the literature, we chose the first scenario and discharged the patient with a diagnosis of migraine. Because of the frequency and severity of attacks, prophylaxis with low dose topiramate was initiated. The WMH observed on MRI were considered clinically insignificant at this stage, but the patient was advised to perform regular neurologic follow-up consultations and a control MRI scan in one year.

The differential diagnosis of WMH can be difficult, especially if not backed-up by characteristic clinical or laboratory findings. In the present case we preferred the diagnosis of migraine which was best supported by evidences. Care was also taken not to cause unnecessary distress to the patient by communicating an uncertain and unlikely diagnosis, MS, which is traditionally perceived as a certain stigma. Nevertheless, we consider the careful follow-up essential in such cases, as the additional data gathered in the course of the disease may direct the clinical thinking toward other, initially neglected diagnostic options.
4. References


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