"Incidentalomas"

How brain MRI can complicate migraine management

Such is the misery migraine can inflict that patients understandably become convinced that "there must be something wrong with my brain". When seeking help from a healthcare provider, some migraine patients feel their evaluation is incomplete if a brain imaging study is not performed. *Why are you short-changing me?* they wonder. Not infrequently, some may demand the study.

Compared to computerized axial tomography ("CT" or "CAT") scans, the anatomical detail and resolution offered by magnetic resonance imaging (MRI) is far superior. In the urgent or emergent setting brain CT is quite sensitive in detecting the presence of acute intracranial bleeding, but on an elective basis the value of brain CT in the evaluation of headache is quite low.

So why not obtain brain MRI for every patient with presumed migraine? This topic was covered in detail in one of this magazine's previous issues but to summarize:

- There is no MRI abnormality that is specific for the diagnosis of migraine
- Put another way, if there is a structural abnormality within the nervous central nervous system that is specifically associated with migraine, routine MRI is not a method for detecting that abnormality
- Accurate diagnosis of migraine depends primarily on the history provided by the patient and, to a much lesser extent, the results of a physical examination that focuses on the nervous system
- Diagnostic testing is useful only for excluding other disorders which may mimic migraine
- Given the extremely low likelihood of brain MRI changing diagnosis, treatment and clinical outcome in the patient with historical and physical exam findings consistent with migraine, routine brain MRI would represent a poor use of healthcare resources (36 million Americans with active migraine x 1 MRI scan each @ $3,000 per scan = slightly over $100 billion)
- Most relevant to this article, MRIs performed on migraine patients for no other reason than "to put the patient's mind at rest" may have the opposite effect

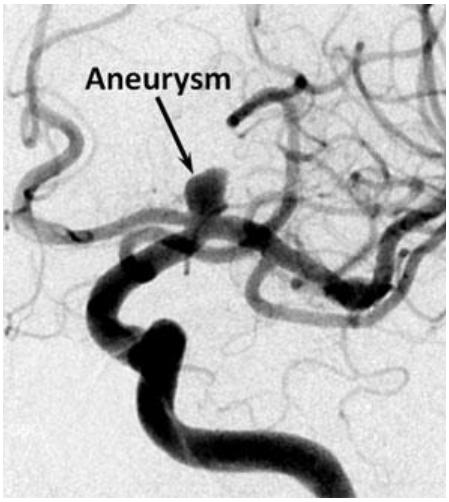
As regards this last bullet point, brain MRI is so sensitive that the imaging study often will detect anatomical abnormalities and variations that are ***incidentalomas***: findings that are unrelated to the patient's headache disorder and in most cases have no clinical significance. Common examples of such incidentalomas include:

- Asymptomatic/unruptured brain aneurysm

- Arnold-Chiari malformation
- Pineal cyst
- Other cysts
- "Empty sella"
- Cavernous malformation
- Meningioma
- "UBOs"

Brain Aneurysm

The prevalence of asymptomatic brain aneurysm in the general population is approximately 3%. Brain MRI is sensitive for detecting aneurysms even as small as 5mm in diameter, and if brain MRI is performed on 100 migraineurs, 3 scans are likely to demonstrate an *incidental* aneurysm unrelated to the individual's headache disorder. The risk of an asymptomatic aneurysm eventually rupturing and causing clinically significant intracranial (usually *subarachnoid*) bleeding depends upon the aneurysm's size and location, with the annual risk of bleeding ranging from as low as near-zero (for small aneurysms in favorable locations) up to as high as 50:50 (for very large aneurysms in unfavorable locations). In younger patients who have aneurysms >7mm in diameter, surgical clipping or a non-surgical, catheter-based procedure often is recommended so as to eliminate the risk of aneurysm.



So, is it good or bad for brain MRI to demonstrate an incidental aneurysm? A tough question to answer. If one is young and the aneurysm is large and unfavorably located, the risk of a life-threatening rupture with intracranial bleeding may be so high that the risk:benefit ratio clearly points to the need for therapeutic elimination of the aneurysm. In other cases (and there are many, many cases that fall within this category), the asymptomatic aneurysm is small or of "borderline" size, and its identification may provoke in the affected patient an uncomfortable degree of chronic stress (*I have time bomb ticking in my head*) which is disproportionate to the actual risk posed by the aneurysm.

Pineal Cysts

Notable for its position precisely in the center of the brain and for its pine cone shape, the tiny pineal gland spans no more than 1/3rd of an inch. Despite its modest size, however, over the centuries the pineal has been extolled as "the third eye" and even "the seat of the soul".

The reality is far less glamorous. The gland secretes a single hormone, melatonin, and does so in rhythm with our exposure to light and darkness. By this mechanism the pineal gland plays a major role in regulating the sleep/wake cycle.

Sometimes it seems as if the pineal glands were created simply to develop cysts (small fluid-filled spaces) that are detected when brain MRI is performed for reasons completely unrelated to the gland and its function. Understandably alarmed by its mention in the MRI scan's formal report ("I have a cyst in my brain!"), worried patients understandably look to their healthcare providers. Depending upon the provider's experience, unnecessary medical evaluations and prolongation of the patient's concern may follow.

Pineal cysts are common, occurring in about 2% of the general population, and are particularly common in females between 20 and 30 years of age, a demographic group in whom migraine is especially prevalent. That the cysts are rarely found in females prior to puberty or following menopause suggests that sex hormones may predispose to their development.

"There is no MRI abnormality that is specific for the diagnosis of migraine."

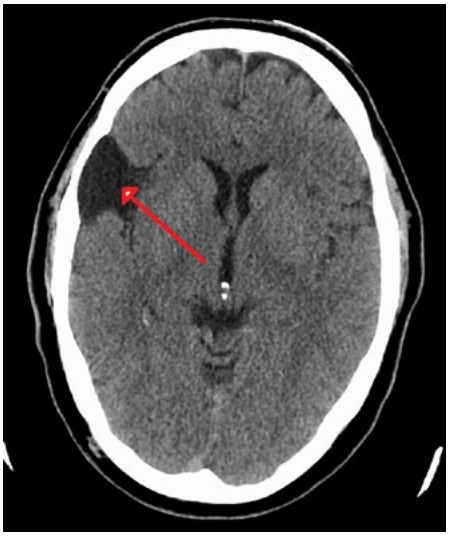
It is extremely unusual for pineal cysts to cause symptoms, headache included, and by far the most common medical intervention required after a cyst is detected is simple reassurance. In a small minority of cases, and typically when the cyst measures more than 2 cm in size, follow-up imaging is performed to exclude progressive enlargement. While pineal gland tumors do occur, they are exceedingly less common than pineal cysts.

Other Cysts

There are many other types of brain cysts that are at least as common as pineal cysts, just as unlikely to cause neurologic symptoms, and typically of no clinical consequence. *Arachnoid cysts* are particularly common.

The arachnoid is part of the meninges, the three-layered membrane that covers the brain, and fluid collections contained within an envelope of arachnoid are frequently seen when brain MRI or CT is performed. While arachnoid cysts be congenital (ie, "born with") or may form as a result of trauma or other types of brain injury. Rarely are they symptomatic, and rarely do they require any treatment, surgical or otherwise.

The photograph is from a brain CT scan demonstrating a typical arachnoid cyst [red arrow].



Brain CT scan demonstrating an arachnoid cyst [red arrow]

UBOs

The most commonly encountered and vexing MRI incidentaloma encountered in a headache clinic is the "UBO" (or, as they typically are multiple, "UBOs").

The acronym stands for "unidentified bright objects", and in MRI parlance the UBOs are areas of small areas of increased signal intensity found in the white matter of the brain [see photo- arrow points to a UBO]

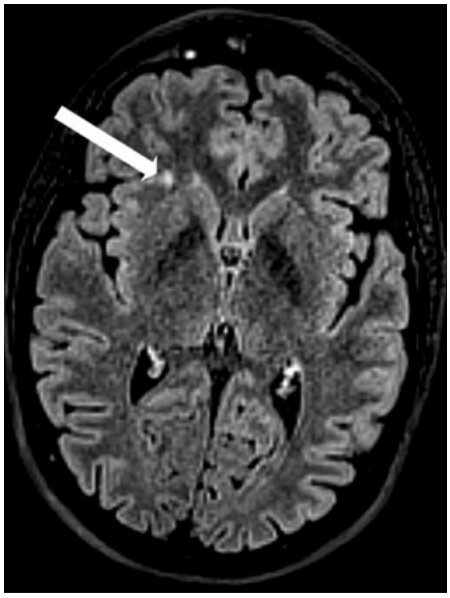
The white matter, which is the darker inner area of the brain depicted in the two photographs shown here, contains the wiring that connects brain neurons with other neurons located in the same hemisphere, neurons in the opposite hemisphere, or neurons located southward in the deep areas of the brain, the stem of the brain or the spinal cord.

When MRI began to be used clinically in the early 1980s, many of the scans performed demonstrated small punctate areas of so-called increased signal (showing up as white on MRI) within the white matter of the hemispheres. This created quite a stir. Did these "UBOs" signal that the patient had multiple sclerosis? if not, then what? As similar white matter changes occur more commonly in patients with stroke risk factors such as hypertension, many felt they might represent small areas of stroke injury.

Bottom line? We still do not know the precise origin of these UBOs, and chances are good that they result from a variety of different causes. Interestingly, they are seen more commonly on the brain MRI scans of individuals with migraine.

The results of the CAMERA-1 study performed in the Netherlands and published in the medical literature in 2004 indicated that UBOs were present more commonly in females with migraine when compared to age-matched females without migraine and were most prevalent in those female migraineurs with a history of aura. There also appeared to be an association between migraine frequency and the presence of UBOs (more frequent migraine = more likely to have UBOs).

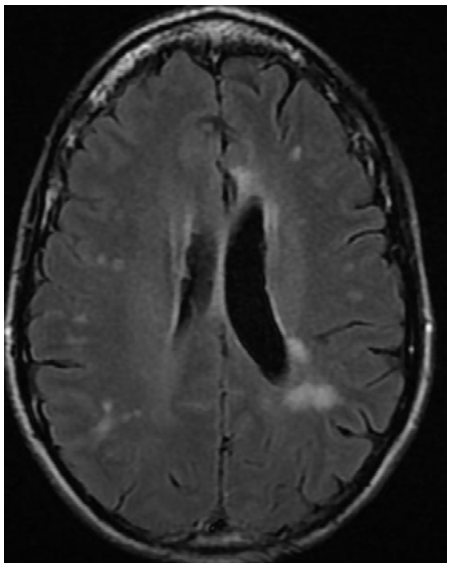
So what? What is the clinical and prognostic significance of UBOs present on the MRI scans of so many female migraineurs? The same Dutch research population was re-studied nine years later, and while the number of UBOs present on MRI had increased in a high percentage of those who had UBOs on MRI 9 years prior,



MRI scan demonstrating a single "UBO" [white arrow] in the brain white matter

the likelihood of developing more UBOs was no greater in individuals with more clinically severe then it was in those with clinically mild migraine. Of more comfort to patients, there was no correlation between the presence of UBOs and evidence of early dementia in the UBO/ migraine population compared to age and gender matched individuals without MRI evidence of UBOs.

In short, from what we know to date, UBOs appear to be no more than a marker of migraine and have no more clinical significance than the presence of freckles on one's face. There is no evidence that in migraineurs these MRI findings indicate an increased risk of developing stroke, dementia, or any other significant neurologic disorder. They do not even appear to correlate with migraine severity or to predict a more negative clinical course as regards the headache disorder itself.



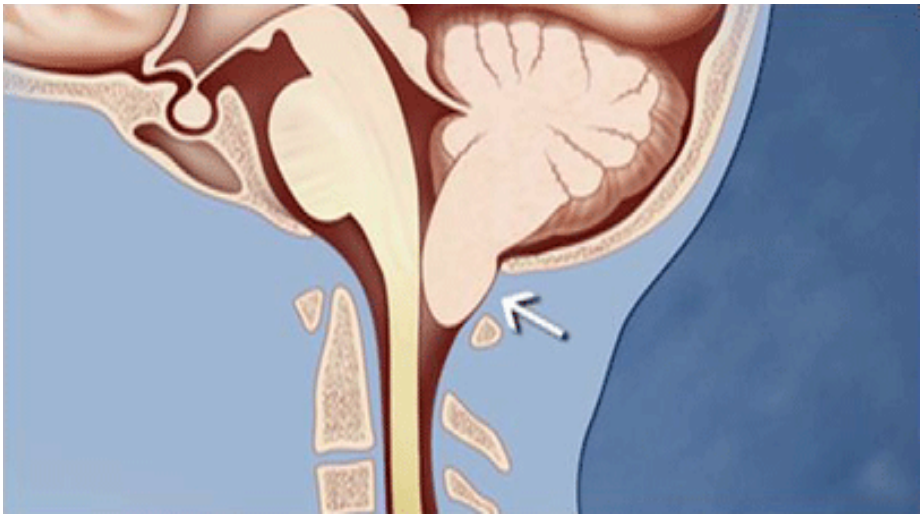
MRI demonstrates multiple "UBOs"

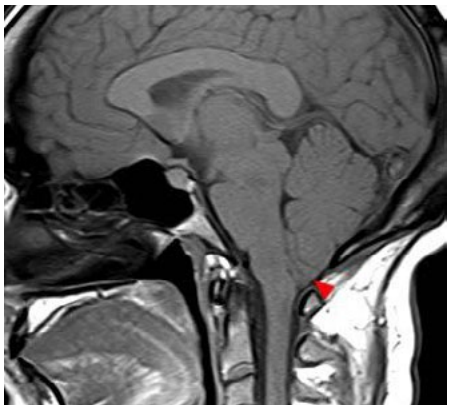
What we *do* know is that when UBOs are detected by MRI, much unnecessary concern, commotion and cost can result. If you have migraine and if you undergo brain MRI that demonstrates these white matter findings, consider consultation with someone skilled in the practice of headache medicine before you embark upon a long, inconvenient, expensive and ultimately pointless journey to rule out multiple sclerosis or another neurologic disease that you thankfully do not have.

Arnold Chiari Malformation

An Arnold-Chiari malformation is a congenital ("born with") abnormality involving the foramen magnum, the large opening at the base of the skull, and the structures passing through and adjacent to that opening: the lower part of the cerebellum, the stem of the brain and the portion of the upper spinal cord that connects to the brain stem like two large cables joining together.

When one has an Arnold-Chiari malformation, the lower portion of the cerebellum (an "old" portion of the brain that is key to maintaining our balance and coordinating our movements) is pulled down through the foramen magnum to crowd and compress other structures in the immediate vicinity (the lower brain stem and upper cervical spinal cord). This is demonstrated in the illustration.





Brain MRI shows cerebellar tissue extending downward towards spinal cord [red arrow]

The malformation may cause a variety of symptoms, including headache. The characteristic headache associated with an Arnold-Chiari malformation involves sudden, severe and short duration pain that may be provoked by coughing, sneezing, straining during a bowel movement, heavy lifting or bending forward…all activities which transiently increase intracranial pressure and by doing so also increase the baseline compression existing within the foramen magnum.

While the true prevalence of Arnold-Chiari malformation in the general population is unknown, published reports indicate its presence on approximately 1 in 1000 brain MRI scans. While that may seem a low rate, if the prevalence of chronic migraine in the US is as high as 6 million, if roughly half of individuals with chronic migraine seek medical attention and if half of them undergo brain MRI as part of their headache evaluation, just in the chronic migraine patient population Arnold-Chiari malformations will be detected by MRI in about 3000.

The sagittal (sideways) views of the brain offered by MRI are quite sensitive for picking up anatomical evidence of cerebellar tissue protruding below the foramen magnum purposes [see photo; red arrow indicates protruding cerebellar tissue]. Those MRI scans often are performed in the course of a diagnostic evaluation for headache.

Only rarely, however, is the Arnold-Chiari malformation demonstrated by MRI responsible for the patients headache disorder or, for that matter, of any clinical consequence whatsoever. The typical headache specialist will see hundreds of patients with this brain MRI finding before encountering that rare patient whose headaches result from Arnold-Chiari malformation or is otherwise symptomatic consequent to the malformation. Only twice in a career spanning decades can this author, a neurologist with a sub-specialty interest in headache, recall recommending surgical decompression of that area for symptomatic Arnold-Chiari malformation.

In short, like pineal and arachnoid cysts, UBOs and even asymptomatic brain aneurysms, this is yet another commonly encountered MRI finding that produces concern and further diagnostic testing that is unnecessary. Even worse, at times it may lead to a major neurosurgical procedure that is of no benefit to the patient. If you find that your brain MRI scan demonstrates an "Arnold-Chiari malformation", take this with a large grain of salt and consult with a headache subspecialist before embarking upon a management strategy that is inappropriately aggressive. For the vast majority of patients, that consultation will result in reassurance, a more accurate diagnosis for the headache disorder involved and an appropriate management strategy.

Summary

These are only four of the many incidentalomas that may be detected by brain MRI. As low tech as it may seem, the best means for diagnosing a headache disorder is a complete history and physical examination performed by someone knowledgeable in the field of headache medicine. Brain MRI, CT and other diagnostic studies are required only in a small minority of patients presenting electively for evaluation of headache. Along with representing a poor use of healthcare resources, "routine" brain imaging "just to be sure" may lead to the detection of incidentalomas that do nothing but alarm patients and lead to unnecessary diagnostic and therapeutic intervention.

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89.7% of patients studied chose Nerivio® instead of medication to treat their migraine attacks[1]

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4 I WANT TO BREAK THE CYCLE OF MEDICATION OVERUSE HEADACHES

Overuse of medications can lead to Medication Overuse Headaches. Treating your migraines with Nerivio®, an effective medication free option, may help break the cycle

References:

1. Marmura MJ, Lin T, Harris D, Ironi A, Rosen NL. Incorporating Remote Electrical Neuromodulation (REN) Into Usual Care Reduces Acute Migraine Medication. Use: An Open-Label Extention Study. Frontiers in Neurology. 2020; 11 :226

2. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ilroni A, Harris D, Lin T, Silberstein SD. Remote Electrical Neuromodulation (REN) Relieves Acute Migraine: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. Headache. 2019;59(8/: 1240-1252.

Mechanism of Action (MOA) Video
Andrew Blumenfeld, MD 2020

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