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Expert Opinions

Incidental Findings and Normal Anatomical Variants on MRI of the Brain in Adults for Primary Headaches

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When MRI scans of the brain are obtained for evaluation of primary headaches in adults, incidental findings are commonly present. After a review of the prevalence of incidental findings and normal anatomical variants, 21 types are presented.

Key words: MRI of the brain, incidental findings, normal anatomical variants, headache, unruptured saccular intracranial aneurysms, Chiari malformation, empty sella turcica, pineal cysts, radiologically isolated syndrome

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About 90% of all headaches are the primary type where MRI scans of the brain will not reveal any pathology responsible for headaches. MRI scans are frequently done for primary headaches for a variety of reasons including the following: secondary pathology; at the patient's or family's request; to reassure the patient, "our stubborn quest for diagnostic certainty;"[1] faulty cognitive reasoning; the medical decision rule where it is better to impute disease than to risk overlooking it; busy practice conditions where tests are ordered as a shortcut; financial incentives; professional peer pressure where recommendations for routine and esoteric tests are expected as a demonstration of competence; and medicolegal concerns.[2] Incidental findings are common, often revealing benign pathology which may cause concern of the patient. Normal anatomical variants are also common.[3] Definitions may differ among investigators as some may classify normal anatomical variants as incidental findings while others may not.[4]

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CASE HISTORY

Case 1.—This is a 32-year-old male with a history of increasingly frequent episodic migraine. MRI of the brain was normal except for a 7 mm pineal cyst. Another MRI of the brain 5 years later for chronic migraine showed no change in the size of the cyst.

Case 2.—This is a 27-year-old male, the brother of case 1, with a history of headaches consistent with migraine without aura since childhood. Headaches have increased to twice a week in frequency. Past medical history is negative. Neurological examination is normal. Magnetic resonance imaging (MRI) of the brain shows a left anterior cranial fossa arachnoid cyst measuring 1.2-cm anteroposterior by 1.6-cm transverse by 1.5-cm craniocaudad without significant parenchymal compression. He is placed on a triptan with a good response.

Questions.—How often and which incidental findings (IF) are present in adults without neurological

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problems and migraineurs? In alphabetical order, what are some incidental findings and anatomical variants which may be encountered?

EXPERT OPINION

How Often and Which Incidental Findings Are Present in Adults?—There have been a number or studies which report IF in normal volunteers with the prevalence of clinically significant neuropathologies occurring in 2-8% of the general population.[5]

In a meta-analysis of 16 studies of 19,559 people with a range of 1-97 years without neurological symptoms who underwent MRI of the brain with or without contrast for research purposes or for occupations, clinical, or commercial screening, the overall prevalence of IF was 2.7% (4.3% in studies where participants underwent at least one high resolution MRI sequence versus 1.7% in studies using only low resolution sequences).[6] White matter hyperintensities, silent brain infarcts, brain microbleeds, and anatomical variants were not included. The following IF and prevalences (%) were found: neoplasia, 0.7 (meningioma, 0.29; pituitary adenoma, 0.15; low grade glioma, 0.05, acoustic neuroma, 0.03; lipoma, 0.04; epidermoid, 0.03); structural vascular abnormalites, 0.56 (aneurysm, 0.35; cavernous malformation, 0.16; arteriovenous malformation 0.05); inflammatory lesions, 0.09 (definite demyelination, 0.06; possible demyelination, 0.03); cysts, 0.54 (arachnoid cysts, 0.5; colloid cyst, 0.04), Chiari I malformation, 0.24; hydrocephalus, 0.10; and extra-axial collection, 0.04.

In a study of 206 healthy volunteers ages 9-50 years (mean 25.68 years) on a 3-tesla MRI scanner, 19% had incidental findings.[7] IF without clinical importance were present in 9% as follows: signal abnormalities, 4%; pineal cysts <1 cm, 3%; and mega cisterna magna, 1%. IF with clinical importance were present in 10% as follows: intrasellar abnormalities, 6%; pineal cysts >1 cm, 2%; cavernomas, 1%; arteriovenous malformations, 1%; multiple white matter lesions, 1%; Chiari malformation, 1%; subependymal heterotopia, .5%; and multiple sinusoidal polpys, 1%.

In a study of 203 healthy volunteers ages 18-35 years (mean 21.9 years) on a 1.5-tesla MRI scanner, 30.5% had variations of the norm including the 3 most common as follows: pineal gland cyst, 6.1%; widened bifrontal subarachnoid space, 6.1%; and Rathke cleft cyst, 3.9%.[8] IF of the brain were found in 9.4% with occasional/not important white matter lesions, 4.4% and Chiari I malformations, 1%. In 180 participants, the upper head and neck region were evaluated, finding 3.3% with variants of the normal (most common hypoplastic frontal or maxillary sinus) and 36.7% with abnormal findings (most common sinonasal retention cyst or polyp, 10%; isolated mucosal swelling, 6.1%; pharyngeal or parotid lymphadenopathy, 5%; and cystic lesion in the parotid gland, 1%.

In a general population study of 1006 participants living in the county of Nord-Trøndelag, Norway, who underwent MRI on a 1.5-tesla scanner, IF were present in 27.1% and clinically relevant findings in 15.1%.[9] Two or more IF were present in 21.8%.

In a general population study of 2000 persons 45-97 years old (mean age of 63.3 years) living in Rotterdam, the Netherlands, on a 1.5-tesla scanner, the following IF and percentages were found: asymptomatic brain infarct, 7.2 (lacunar, 5.6; cortical, 5.6); aneurysms, 1.8; benign primary tumors, 1.6 (meningioma, 0.9; vestibular schwannoma, 0.2; lipoma, 0.2; pituitary tumor, 0.3); malignant primary tumors, <0.1; metastases, <0.2; cavernous angioma, 0.4; subdural hematoma, <0.1; arachnoid cyst, 1.1, Chiari I, 0.9; and major vessel stenosis, 0.5.[10] Asymptomatic brain infarcts were found in the following ages and percentages: 45-59 years, 4; 60-74, 6.8; 75-97, 18.3. The median volume of white matter lesions (mL) were found in the following ages: 1.8, 45-90 years; 3.05, 60-74 years; and 7.74, 75-97 years. All but 3 of the 35 aneurysms detected were smaller than 7 mm and all but 2 were located in the anterior circulation.

Normal anatomical variants are also common, with different studies having varying criteria for separating from IF. In a retrospective study of MRI scans of 666 children (mean age 9.82±, 58% male) seen at a pediatric neurology practice at a tertiary care center, normal anatomical variants were present in 17%, including the following: asymmetric

ventricles, 2.1%; cavum septum pellicidum, 0.5%; cisterna magna enlargement, 0.2%; enlarged periventricular spaces, 3.8%; external hydrocephalus, 0.6%; pineal cyst, 1.8%; variant signal intensity, 3.6%; and white matter abnormalities, 4.5%.[11]

In a retrospective study of MRI scans of 2536 healthy young men (ages 17-35 years, mean 20.5 years), normal anatomical variants were present in 18.45% as follows: cavum vergae, 4.77%; large basal cisterns, 1.74%; pineal gland cysts, 3.43%; enlarged perivascular spaces, 2.56%; asymmetry of the lateral ventricles, 2.68%; occasional white matter lesions, 2.6%; ossification of the cerebral falx, 0.32%; and empty sella, 0.35%.[12]

In the Norwegian county study of 1006 participants, heterotopia was present in 0.2%, mega cisterna magna in 0.1%, and septum pellicudum/cavum vergae in 0.7%.[9]

In Alphabetical Order, What Are Some Incidental Findings and Anatomical Variants Which May Be Encountered?—*Aneurysms.*—Patients are often concerned that they have an unruptured saccular intracranial aneurysm (UIA) as the cause of their migraine or tension-type headache. UIAs may be found as an incidental finding when obtaining MRI scans for headache and greater detection when MRA or CTA scans are also obtained. About 3.2% of the adult population has an UIA, which develops over the life course, in a population without comorbidity with a mean age of 50 years.[13] There is a higher prevalence ratio in those aged 30 years or older, in females compared to males (1.61 with a ratio of 2.2 in those more than 50 years), with a positive family history, and in those with hypertension, hyperlipidemia, smoking, and autosomal dominant polycystic kidney disease. About 20-30% of those with UIAs have more than one.

In a meta-analysis, the site of UIAs was as follows: anterior cerebral artery and branches, 18%; middle cerebral artery (MCA), 35%; internal carotid artery (ICA), 32%; posterior communicating artery (PCA), 10%; and vertebrobasilar arteries, 5%.[13] Common anterior circulation sites include the junction of the ACA with the anterior cerebral, the junction of the PCA with the ICA, and the bifurcation of the MCA. Common posterior circulation sites include the top of the basilar artery, the junction of the basilar and the superior or anterior inferior cerebellar arteries, and the junction of the vertebral artery and the posterior inferior cerebellar artery. Sixty-six percent of aneurysms were less than 5 mm. Aneurysmal growth is variable with some UIAs unchanged for a long time before undergoing rapid growth and some developing and rupturing within weeks or months, with up to 45% growing over a 19 year period.[14]

Risk factors for triggering UIA rupture include straining for a bowel movement, use of caffeine, episodes of anger, startling, sexual intercourse, nose-blowing, and vigorous physical exercise with a range of relative risk from 2 for coffee intake to 20 for startling. These triggers induce a sudden and short increase in blood pressure. However, it is not clear that avoiding these triggers has any significant effect on the risk of rupture. For example, those with UIAs would need to avoid 1.3 million episodes of sexual intercourse to avoid one aneurysm rupture. Treatable risk factors are cigarette smoking and hypertension.

Size of the UIA is the most significant risk factor for rupture. The hazard ratio of rupture as compared to aneurysms <5.0 mm increases with increasing size as follows: 5.0-6.9 mm, 1.1; 7.0-9.9, 2.3; 10.0-19.9, 5.5; ≥20.0 cm, 20.8. In one prospective study of those with UIAs <5 mm in size, the average annual rupture rate was 0.34% for single aneurysms and 0.95% for those with multiple aneurysms.[15] However, it is not possible to estimate the long-term risk of rupture by multiplying the risk of rupture and estimating the remaining years of life remaining because growth and rupture are not constant over time and the risk of rupture may decline over time. In a long-term follow-up study, all ruptures occurred within the initial 25 years of follow-up.[16]

Interventional treatment should probably be provided for large UIAs and those with posterior circulation or PCA aneurysms. For patients under the age of about age 60, the optimum management of small (<7 mm) anterior circulation aneurysms in not known with certainty.[17] Conservative medical management with smoking cessation, treatment of hypertension, and follow-up MRA or CTA can be

considered although intervention might be considered in those <50 years of age with a strong family history of subarachnoid hemorrhage or aneurysm. The optimum interval for follow-up scans is not known but one recommended approach is to obtain the first follow-up scan after 6-12 months and then annually for 1-3 years and every 2-5 years following if the aneurysm is clinically and radiologically stable.[18]

Patients with primary headaches are particularly concerned when they have a family member with a history of intracranial aneurysm. In a screening study of relatives of patients ages 20-70 years of age with subarachnoid hemorrhage, 4% of screened first-degree relatives had a UIA.[19] In another study, the age-adjusted prevalence of intracranial aneurysm was 9.2% among first-degree relatives aged 30 years or older in families with 2 or more affected members.[20]

Radiological screening with MRA (or CTA if contraindications to MRA) for aneurysms is generally recommended in patients with a history of 2 or more first-degree relatives with aneurysms or subarachnoid hemorrhage (SAH)[17] yearly for 3 years and then every 5 years for those who had no aneurysms on the initial scans.[21] Screening is recommended for patients with autosomal dominant polycystic kidney disease who have a family history of aneurysm or SAH. The American Heart Association/American Stroke Association recommendation is as follows: "It may be reasonable to offer noninvasive screening to patients with familial (at least 1 first-degree relative) aneurysmal SAH and/or a history of aneurysmal SAH to evaluate for de novo aneurysms or late regrowth of a treated aneurysm, but the risks and benefits of this screening require further study (Class IIb; Level of Evidence B)."[22]

Arachnoid Cysts.—The most common congenital cyst abnormality in the brain, found in 1.1% in a population based study of people ages 45-97.[10] Consist of confined diverticula from the natural septations of the arachnoid member and are filled with cerebrospinal fluid (CSF). A recent "Expert opinion" reviews the relationship with headache and management.[23]

Cavum Septum Pellucidi (CSP) and Cavum Vergae (CV).—Both are anatomical variants.[24] The CSP, which is part of normal development, is the space between the two leaflets of the septum pellucidum, which has been reported as persisting in adults in 3-60% of cases. The CV is the continuation of the CSP posterior to a coronal plate through the columns of the fornix. The CV is a horizontal cleft that is formed between the commissura fornicis and the corpus callosum when the two commissural plates fail to fuse completely during fetal development with a prevalence of 0.4-3% often present along with CSP.

Cerebral Vascular Malformations.—The relationship of cerebral vascular malformations including developmental venous anomalies, arteriovenous malformations, cerebral capillary telangiectasias, cavernous malformations, cerebral arteriovenous fistulas, and headache are reviewed in a recent "Expert opinion."[25]

Chiari Malformations.—Imaging prevalence of about 1% of adults.[26] In a retrospective review of 22,591 patients who underwent MRI imaging of the head and cervical spine at one institution over 43 months, 175 (0.8%) were found to have Chiari type I malformation (CM1) with tonsillar herniation extending more than 5 mm below the foramen magnum (age specific or age group-specific prevalence not reported).[27] The average extent of ectopia was 11.4 ± 4.86 mm. Fourteen percent were clinically asymptomatic. Syringomyelia and osseus anomalies were found in only one asymptomatic patient.

Tonsillar position is not static over the years. In a study of 2400 patients who underwent MRI of the brain for any reason, mean cerebellar tonsil position descended with advancing age into young adulthood and then ascended with advancing age through adult life. Those with tonsil position at the low end of this distribution are within the group consistent with an imaging diagnosis of CM1.[28]

Adults with symptomatic CM1 present with headache and neck pain in 73%.[29] The headache is a cough type which is usually occipital and can also be precipitated by neck flexion usually lasting less than 5 minutes."[30] CM1 is not associated with primary episodic headaches (with the rare exception of basilar migraine-like cases).[31] There is no clear

evidence supporting an association of CM1 with chronic daily headache.

Empty Sella Turcica.—Secondary empty sella usually is due to a pituitary adenoma that shrinks after treatment or spontaneous regression but can also be due to postpartum pituitary necrosis (Sheehan syndrome) or lymphocytic hypophysitis.

Primary empty sella (PES) is due to intrasellar herniation of the suprasellar arachnoid and subarachnoid space cerebrospinal fluid resulting in flattening of the pituitary gland.[32] Partial empty sella occurs when less than 50% of the sella is filled with CSF and total when more than 50% of the sella is filled with CSF and the pituitary gland thickness is <2 mm.[33] Most cases are primary due to a normal variant with an anatomical defect of the diaphragma sella (a fold of dura mater pierced by the infundibulum to connect the pituitary to the hypothalamus) that separates the CSF filled subarachnoid space from the pituitary that is present in up to 50% of adults. The presence of empty sella ranges from 5.5 to 35% with a female/male ratio of 4/1 and is more common in middle aged multiparous women and in obesity.[34]

Empty sella occurs in up to 85% of patients with pseudotumor cerebri, recently found to be due to chronic elevation of the intracranial pressure associated with enlargement of the sella turcica, which contributes to the partially empty appearance.[35] There is little or no reduction in the size of the pituitary gland, which becomes molded to the walls of the larger sella.

Occasionally, herniation of the suprasellar visual system and the anterior region of the third ventricle can occur with PES resulting in visual disturbances in 1.6-16%[34] of cases but has also been rarely reported in cases without visual system herniation.[36]

In 8-60% of cases, different degrees of hypopituitarism have been reported, which can be explained by chronic compression of the pituitary gland and stalk by CSF. Hyperprolactinemia and growth hormone deficiency are the most common pituitary disorders associated with PES. The authors of one study recommend endocrine and neuro-ophthalmological evaluations for patients with PES.[34]

Gray Matter Heterotopia.—Interruption of normal neuronal migration from near the ventricle to the cortex with normal neurons in abnormal locations.[37] The most common form is subependymal with nodules of gray matter immediately beneath, the ependyma of the lateral ventricles usually causing seizures but has a prevalence of 0.5% in healthy volunteers ages 9-50 years.[7]

Mastoiditis.—Increased fluid signal in the mastoid air cells on T2-weighted images on MRI is sometimes interpreted as due to mastoiditis in otherwise asymptomatic patients who may be referred to primary care physicians or otorhinolaryngologists for further evaluation. In a retrospective study of 275 patients (ages 19-82, mean 45.5 years) diagnosed with mastoiditis on MRI scan where otolaryngologic evaluations were available, 9% had acute, serous or chronic otitis media, 7% had eustachian tube dysfunction, and 2% had tympanosclerosis.[38] The remainder had normal physical otological findings.

In a study comparing 35 adults and pediatric patients with clinical acute mastoiditis and 34 age-matched controls, acute mastoiditis usually demonstrated hypointense to CSF intramastoid T2-weighted signal intensity and diffusion restriction and intense intramastoid enhancement were absent in incidental mastoid effusion.[39] Intramastoid T2-hyperintensity alone is not a reliable sign for acute mastoiditis.

Mega Cisterna Magna.—A normal variant with a focal enlargement of the subarachnoid space in the inferior and posterior portions of the posterior fossa present in about 1% of the population.[7]

Meningioma.—Term coined by Harvey Cushing.[40] Annual incidence of 7.61 per 100,000 population accounting for 20% of all primary tumors, with about 26,000 new cases per year in the United States. Meningiomas occur two times more often in women, than in men, with an increasing incidence with older age. Twenty-five percent are symptomatic on presentation, with headache being the most common presenting symptom in 36%. Headaches are commonly associated[41] with tension-type more frequent than migraine-like, occurring daily in 31% and less than weekly in 22%.[42]

Many meningiomas will not grow. In a retrospective population based study, among 67 asymptomatic patients followed up for more than 5 years, 63% did not have tumor growth.[43]

Most small (up to about 2 cm in diameter) incidental meningiomas can be observed with a follow-up scan in 3-6 months.[44] If no change in size and asymptomatic, follow-up scans once a year for 3-5 years and then every 2-3 years for as long as they would be considered for treatment.

Normal Variants of the Cerebral Circulation.—Some headache patients such as those with thunderclap headaches will undergo MRA or CTA to exclude a vascular cause and any of numerous normal variants of the cerebral circulation are found.[45] Some will be reviewed.

A duplication is two distinct arteries with separate origins and no distal arterial convergence. The prevalence of anterior communicating artery duplication is 18% and middle cerebral artery, 0.2-2.9%.

A fenestration is a division of the arterial lumen into distinctly separate channels, each with its own endothelial and muscularis layers while the adventitia may be shared due to abnormal development of primitive embryological vessels. There is an association of fenestration and aneurysm formation, which may be due to turbulent flow but no definite pathological relationship.[46] Fenestrations are more common in the vertebrobasilar arteries than in the anterior circulation.

There are many normal variants of the circle of Willis. An azygos ("single") anterior cerebral artery, with a prevalence of 0.2-4%, is persistence of the embryonic medial artery of the corpus callosum resulting in supply of the bilateral anterior cerebral territories by a single midline A2 trunk. Occlusion can cause ischemia in both hemispheres. A persistent trigeminal artery, with a prevalence of 0.1-0.6%, originates immediately from the internal carotid artery after its exit from the carotid canal, can follow a para (lateral type) or intrasellar course (medial type) and anastomoses with the mid-basilar artery. A persistent hypoglossal artery, with a prevalence of 0.02-0.10%, originates from the internal carotid artery at the levels of the C1-3 vertebral bodies, travels through the hypoglossal canal, and anastomoses with the basilar artery. This variant can cause glossopharyngeal neuralgia.

Paranasal Sinuses.—Incidental paranasal sinus abnormalities are common. In a population-based study of 982 people (518 females; mean age of 58.5 years, range 50-66) living in a county in Norway, MRI scans showed opacifications (mucosal thickening, polyps, retention cysts, and fluid level $\geq$1 mm) in 66% with mucosal thickening in 49%, commonly in the maxillary sinuses (29%).[47] Opacifications also occurred as follows: anterior ethmoid, 23%; posterior ethmoid, 21%; frontal sinus, 9%; and sphenoid, 8%. Polyps and retention cysts were mainly in the maxillary sinuses in 32%. Fluid was present in 6%. Migraine, tension-type headache, and unclassified headache were not associated with an increased degree of paranasal sinus opacification.[48]

Incidental paranasal sinus disease has also been studied in younger adults. In a study of 115 patients undergoing imaging for non-sinus-related diagnoses, 47% underwent CT (mean age52.3 ± 22.4 years) and 53% MRI of the head (38.5 ± 18.4 years). MRI was more sensitive than CT to detect sinus mucosal abnormalities.[49] The prevalence of incidental sinus abnormalities was between 14.8% and 37% for CT and 29.5% and 85.2% depending upon the cutoff Lund-Mackay Grading System used. There was no significant difference between different age groups or genders.

Pineal Cysts.—Found in up to 6.1% of healthy young volunteers.[8] Migraines may be more common in those with pineal cysts.[50] In a study of 51 patients with pineal cysts, headaches were present in 51% (half with migraine) as compared to 25% of controls.[51]

Al-Holou et al obtained follow-up MRI imaging in 151 patients (108 females) with pineal cysts with a mean age of 40.1 ± 14.5 years for 6 months to 13 years with a mean of 3.4 years.[52] Most cysts were stable in size and no patients developed clinical symptoms. There was an increase in size in 4 and decrease in 23. Follow-up imaging and neurosurgical evaluation was not believed to be mandatory or adults with asymptomatic cysts.

Out of 281 patients with incidental pineal cysts (median age 38 years [range 16-84 years] and 63.3% female), Nevins et al obtained follow-up

MRI imaging in 181 patients with pineal cysts with a median length of follow-up of 6 months (range 1-68 months).[53] During the follow-up period, 11 (6%) changed in size with a reduction in size in 4 and an increase in size in 7. No patients developed complications. They suggested a single follow-up MRI at 12 months and, if the cyst was stable, no further follow-up. If the cyst was significantly larger or the diagnosis was not certain, additional follow-up at the discretion of a neurosurgeon.

Pituitary Tumors.—Incidence of 3.47 per 100,000 accounting for 15% of adult brain tumors occurring more often in females than males and with increasing age.[54] Pituitary adenomas can cause or be associated with headaches.[55] Pituitary tumors can cause symptomatic cluster headache.[56] In a prospective study of 84 patients with pituitary tumors and headaches, the following diagnoses were made: chronic migraine, 46%; episodic migraine, 30%; primary stabbing headache, 27%; short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing, 5%; cluster headache, 4%; hemicrania continua, 1%; and headaches which did fit any International Classification of Headache Disorders criteria, 7%.[57]

An author provided guidelines for evaluation and follow-up of incidental pituitary adenomas.[58] For adenomas <10 mm, measure only serum prolactin if there is no clinical suspicion of hormonal hypersecretion. For lesions between 5 and 9 mm in diameter, yearly MRI for 2 years and, if stable, decreased to every few years and then less often. For lesions 2-4 mm in diameter, no further imaging. For adenomas ≥10 mm without neurological symptoms or hormonal hypersecretion, hormonal testing for hyper- and hyposecretion, visual testing, and pituitary MRI at 6 and 12 months during the first year is recommended. Patients with lesions causing visual impairment or other neurological symptoms can be considered for surgery. Treatment of pituitary lesions ≥10 mm and symptoms related to clinically important hormonal hypersecretion depends upon the type of adenoma.

Radiologically Isolated Syndrome.—When white matter abnormalities are present, the patient may be concerned as to whether they have multiple sclerosis even though they have no symptoms. The term "radiologically isolated syndrome" (RIS) was coined by Okuda et al[59] to apply to incidental MRI findings of white matter lesions suggestive of multiple sclerosis showing dissemination in space (Barkhof's criteria) in subjects with a normal neurological exam and without a history of typical multiple sclerosis symptoms. The MRI diagnostic criteria are the following: ovoid, well-circumscribed, and homogeneous foci with or without cerebellar involvement; T2 hyperintensities measuring >3 mm and fulfilling at least three out of four Barkhof criteria, which are (1) nine or more lesions or one or more gadolinium-enhancing lesions, (2) three or more periventricular lesions, (3) one or more juxtacortical lesions, and (4) one or more infratentorial lesions; and the CNS white matter anomalies are not consistent with a vascular pattern.

RIS may be quite uncommon. A hospital-based study found a prevalence of 0.15% among those ages 15-40 years who had undergone an MRI of the brain for a variety of medical symptoms.[60] In a county in Sweden with a high incidence of multiple sclerosis (the incidence rate in Sweden is 10.2/100,000 person-years), the incidence rate of RIS was 0.8 cases per 100,000 person-years.[61] Within 5 years after initial RIS detection, up to 30% of RIS patients will develop a symptomatic demyelinating episode and almost two-thirds will progress radiologically with new lesions on MRI.[62] Disease-modifying treatment is not currently recommended for RIS.

In a retrospective review of 326 patients (218 females, mean age of 34.5 years with a range of 10-55 years) having a MRI pre- and post-contrast for headache without a diagnosis of multiple sclerosis or clinically isolated syndrome, the prevalence of white matter hyperintensities was 51.5%.[63] Barkhof "touching" criteria were met in 2.4% and 7.1% met the Barkof 3 mm criteria. McDonald criteria were met in 24.4% for "touching" and 34.5% for 3 mm. The "touching" criteria include periventricular lesions in contact with the ventricles and the 3 mm criteria include periventricular lesions having an edge within 3 mm of the ventricles. By comparison, the prevalence of multiple sclerosis in the general population is 0.085%.

Rathke's Cleft Cysts.—Rathke's pouch, first described by German embryologist Martin Rathke in 1839, is an evagination at the roof of the developing mouth which gives rise to the anterior pituitary. The cysts are benign sellar and suprasellar lesions (most commonly pars intermedia) arising from the epithelial remnants of Rathke's pouch which contain mucoid or gelatinous material within a thin cyst wall.[64] The peak incidence is 30-50 years, with a prevalence in one study of healthy volunteers ages 18-35 years of 3.9%[8] and about 11% in autopsy studies.

Rathke's cleft cysts are usually incidental but can cause symptoms if they are large enough to compress adjacent structures or rupture. Headaches are the most common manifestation occurring in up to 40% of cases as the only symptom and in 33-81% with other symptoms. The headaches are usually episodic (but can be chronic or continuous) non-pulsating frontal, bilateral, or deep retro-orbital (occasional occipital, temporal, or generalized) pain with occasionally associated nausea and vomiting. Between 12-75% of patients report visual disturbance at presentation and often have disturbances in visual acuity and visual field (depending upon the cyst size and compression of the optic nerve or chiasm). Anterior pituitary hormone deficits in one or more axes are present in 19-81% of patients although the prolactin level can be elevated due to stalk effect. Diabetes insipidus at presentation has been variably reported in 0-19% of cases.

Surgery is not required for small asymptomatic cysts. A 9 year follow-up study of incidental cysts found 31% becoming symptomatic with cyst growth, visual loss, or endocrinopathy requiring surgery.[65] Surgery (most commonly transphenoidal fenestration and drainage) is indicated when cysts cause clinical symptoms.

Sagittal Sinus Venous Lake.—A benign, well-defined lucent skull lesion due to remodeled bone that contains venous structures.

Vein of Galen Aneurysm.—Accounting for about 1% of all intracranial vascular lesions, this is aneurysmal dilation of the median prosencephalic vein of Markowski, not the vein of Galen.[66] Adults can present with headache and seizures caused by intraparenchmal or subarachnoid hemorrhage.

Vestibular Schwannomas (Acoustic Neuromas).—Incidence of about 1 per 100,000 person-years with a median age of diagnosis of 50 years. Unilateral in more than 90% of cases and bilateral primarily in those with neurofibromatosis type 2. In a series of 962 patients, the most frequent clinical symptoms were disturbances of the acoustic (95%), vestibular (61%, most often intermittent unsteadiness while walking or vertigo), trigeminal (9%), and facial (6%) nerves.[67] Follow-up scans every 6-12 months may be warranted in some carefully selected patients as most tumors are slowly growing.[68]

In a study of 148 consecutively observed patients with vestibular schwannomas as compared to general population controls, the perceived severity of ongoing headaches was significantly greater in the observation group with the risk of having severe headache disability with a small or medium-sized untreated tumor about twice that of the general population.[69] Headache most commonly lateralizes to the side with the tumor.[70] The explanation for the increased headache disability from a small tumor may be dural traction within the internal auditory canal and at the porus acusticus.

Virchow-Robin Space (VRS).—Described by Virchow in 1851 and Robin in 1859, this is a perivascular space that surrounds small arteries and arterioles as they go from the subarachnoid space and into the brain parenchyma which are most commonly around the lenticulostriate arteries as they perforate the anterior border of the basal ganglia and are also present around the medullary arteries entering the cortex over the high convexities projecting down into the hemispheric white matter and in the mesencephalon.[71,72] VRS have no direct connection with the subarachnoid space. État criblé describes the multiple enlarged VRS most commonly in the basal ganglia with thickened, ectatic, and sclerotic vessel walls.

In a retrospective study of 125 healthy subjects (age 0.5-30 years, median 14 years) with high-resolution image 3D brain scans, VRS was found in all subjects. In a study of 36 patients (ages 2-16 years) using routine sequences, VRS were present

in 80%. In the Norwegian county population-based study of 1006 people between the ages of 5-66 years who had 1.5 T MRI scans, VRS were present in all (except 9 excluded for poor image quality).[72]

Two of the 125 subjects (ages 16 and 24 years) or 1.6% had dilated (focal expansions that were either irregular or ectatic in appearance) VRS as normal variants. However, dilated VRS can be present in the following disorders: metabolic/genetic; vascular; inflammatory; neoplastic; neuroectodermal; mild traumatic brain injury; and miscellaneous including Parkinson's and chronic alcoholism. VRS are not more common in migraineurs from ages 50 to 65 years as compared to headache-free people.[72]

VRS can be mistaken for lacunar infarcts. Dilated VRS are smaller and more round and linear with normal adjacent white matter than the more wedge-shaped lacunar infarcts with a rim of surrounding gliosis on the fluid attenuation inversion recovery sequence. However, there is an overlap in size so it may be difficult to distinguish the two in occasional cases.

White Matter Abnormalities (WMA).—WMA are foci of hyperintensity on both proton density and T2-weighted images in the deep and periventricular white matter due to either interstitial edema or perivascular demyelination.[73] The prevalence ranges from 4-59% in migraineurs and 6-14% in controls.[74] While the cause and clinical significance of WMA in migraineurs is uncertain, various hypotheses have been advanced including increased platelet aggregability with microemboli, abnormal cerebrovascular regulation, and repeated attacks of hypoperfusion during the aura.

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REFERENCES

1. Kassirer JP. Our stubborn quest for diagnostic certainty. A cause of excessive testing. *N Engl J Med.* 1989;320:1489-1491.
2. Evans RW. Diagnostic testing for migraine and other primary headaches. *Neurol Clin.* 2009;27: 393-415.
3. Miller DA, Merinbaum DJ, Kirsch JE, The head. In: Bancroft LW, Bridges M, eds. *MRI Normal Variants and Pitfalls*. Philadelphia: Lippincott Williams & Wilkins; 2009: 1-65.
4. Gupta SN, Gupta VS, White AC. Spectrum of intracranial incidental findings on pediatric brain magnetic resonance imaging: What clinician should know? *World J Clin Pediatr.* 2016;5:262-272.
5. Brown DA, Hasso AN. Toward a uniform policy for handling incidental findings in neuroimaging research. *AJNR Am J Neuroradiol.* 2008;29:1425-1427.
6. Morris Z, Whiteley WN, Longstreth WT, Jr, et al. Incidental findings on brain magnetic resonance imaging: Systematic review and meta-analysis. *BMJ.* 2009;339:b3016.
7. Hartwigsen G, Siebner HR, Deuschl G, Jansen O, Ulmer S. Incidental findings are frequent in young healthy individuals undergoing magnetic resonance imaging in brain research imaging studies: A prospective single-center study. *J Comput Assist Tomogr.* 2010;34:596-600.
8. Reneman L, de Win MM, Booij J, et al. Incidental head and neck findings on MRI in young healthy volunteers: Prevalence and clinical implications. *AJNR Am J Neuroradiol.* 2012;33:1971-1974.
9. Håberg AK, Hammer TA, Kvistad KA, et al. Incidental intracranial findings and their clinical impact; The HUNT MRI study in a general population of 1006 participants between 50-66 years. *PLoS One.* 2016;11:e0151080-
10. Vernooij MW, Ikram MA, Tanghe HL, et al. Incidental findings on brain MRI in the general population. *N Engl J Med.* 2007;357:1821-1828.
11. Gupta SN, Belay B. Intracranial incidental findings on brain MR images in a pediatric neurology practice: A retrospective study. *J Neurol Sci.* 2008;264: 34-37.
12. Weber F, Knopf H. Incidental findings in magnetic resonance imaging of the brains of healthy young men. *J Neurol Sci.* 2006;240:81-84.
13. Vlak MH, Algra A, Brandenburg R, Rinkel GJ. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: A systematic review and meta-analysis. *Lancet Neurol.* 2011;10:626-636.
14. Etminan N, Rinkel GJ. Unruptured intracranial aneurysms: Development, rupture and preventive management. *Nat Rev Neurol.* 2016;12:699-713.

15. Sonobe M, Yamazaki T, Yonekura M, Kikuchi H. Small unruptured intracranial aneurysm verification study: SUAVe study, Japan. *Stroke.* 2010;41: 1969-1977.
16. Juvela S, Poussa K, Lehto H, Porras M. Natural history of unruptured intracranial aneurysms: A long-term follow-up study. *Stroke.* 2013;44:2414-2421.
17. Brown RD, Jr, Broderick JP. Unruptured intracranial aneurysms: Epidemiology, natural history, management options, and familial screening. *Lancet Neurol.* 2014;13:393-404.
18. Singer RJ, Ogilvy CS, Rordorf. Unruptured intracranial aneurysms. In UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed January 21, 2017.
19. Magnetic Resonance Angiography in Relatives of Patients with Subarachnoid Hemorrhage Study Group. Risks and benefits of screening for intracranial aneurysms in first-degree relatives of patients with sporadic subarachnoid hemorrhage. *N Engl J Med.* 1999;341:1344-1350.
20. Ronkainen A, Miettinen H, Karkola K, et al. Risk of harboring an unruptured intracranial aneurysm. *Stroke.* 1998;29:359-362.
21. Singer RJ, Ogilvy CS, Rordorf. Screening for intracranial aneurysm. In UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed January 21, 2017.
22. Connolly ES, Jr, Rabinstein AA, Carhuapoma JR, American Heart Association Stroke Council; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing.; Council on Cardiovascular Surgery and Anesthesia; Council on Clinical Cardiology, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2012;43:1711-1137.
23. Cherian J, Viswanathan A, Evans RW. Headache and arachnoid cysts. *Headache.* 2014;54:1224-1128.
24. Saba L, Anzidei M, Raz E, et al. MR and CT of brain's cava. *J Neuroimag.* 2013;326-335.
25. Kwon PM, Evans RW, Grosberg BM. Cerebral vascular malformations and headache. *Headache.* 2015;55:1133-1142.
26. McVige JW, Leonardo J. Imaging of Chiari type I malformation and syringohydromyelia. *Neurol Clin.* 2014;32:95-126.
27. Meadows J, Kraut M, Guarnieri M, Haroun RI, Carson BS. Asymptomatic Chiari Type I malformations identified on magnetic resonance imaging. *J Neurosurg.* 2000;92:920-926.
28. Smith BW, Strahle J, Bapuraj JR, Muraszko KM, Garton HJ, Maher CO. Distribution of cerebellar tonsil position: Implications for understanding Chiari malformation. *J Neurosurg.* 2013;119:812-819.
29. Pillay PK, Awad IA, Little JR, Hahn JF. Symptomatic Chiari malformation in adults: A new classification based on magnetic resonance imaging with clinical and prognostic significance. *Neurosurgery.* 1991;28:639-645.
30. Arnett BC. Tonsillar ectopia and headaches. *Neurol Clin.* 2004;22:229-236.
31. Riveira C, Pascual J. Is Chiari type I malformation a reason for chronic daily headache. *Curr Pain Headache Rep.* 2007;11:53-55.
32. Saindane AM, Lim PP, Aiken A, Chen Z, Hudgins PA. Factors determining the clinical significance of an "empty" sella turcica. *AJR Am J Roentgenol.* 2013;200:1125-1131.
33. De Marinis L, Bonadonna S, Bianchi A, Giustina GM. Extensive clinical experience. A primary empty sella. *J Clin Endocrinol Metab.* 2005; 90: 5471-5477.
34. Guitelman M, Garcia Basavilbaso N, Vitale M, et al. Primary empty sella (PES): A review of 175 cases. *Pituitary.* 2013;16:270-274.
35. Kyung SE, Botelho JV, Horton JC. Enlargement of the sella turcica in pseudotumor cerebri. *J Neurosurg.* 2014;120:538-542.
36. Guinto G, del Valle R, Nishimura E, Mercado M, Nettel B, Salazar F. Primary empty sella syndrome: The role of visual system herniation. *Surg Neurol.* 2002;l58:42-47.
37. Barkovich AJ, Kuzniecky RI. Gray matter heterotopia. *Neurology.* 2000;55:1603-1608.
38. Polat S, Aksoy E, Serin GM, Yıldız E, Tanyeri H. Incidental diagnosis of mastoiditis on MRI. *Eur Arch Otorhinolaryngol.* 2011;268:1135-1138.
39. Saat R, Mahmood G, Laulajainen-Hongisto A, et al. Comparison of MR imaging findings in paediatric and adult patients with acute mastoiditis and incidental intramastoid bright signal on T2-weighted images. *Eur Radiol. 2016.* 26:2632-2639.
40. Cushing H. The meningiomas (dural endotheliomas): Their source, and favoured seats of origin. *Brain.* 1922;45:282-316.

41. Evans RW, Timm JS, Baskin DS. A left frontal secretory meningioma can mimic transformed migraine with and without aura. *Headache.* 2015; 55:849-852.
42. Schankin CJ, Krumbholz M, Sostak P, Reinisch VM, Goldbrunner R, Straube A. Headache in patients with a meningioma correlates with a bone-invasive growth pattern but not with cytokine expression. *Cephalalgia.* 2010;30:413-424.
43. Yano S, Kuratsu J. Kumamoto Brain Tumor Research Group. Indications for surgery in patients with asymptomatic meningiomas based on an extensive experience. *J Neurosurg.* 2006;105: 538-543.
44. Park JK, Shih HA, Management of known or presumed benign (WHO grade I) meningioma. In UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed January 18, 2017.
45. Parmar H, Sitoh YY, Hui F. Normal variants of the intracranial circulation demonstrated by MR angiography at 3T. *Eur J Radiol.* 2005;56:220-228.
46. Cooke DL, Stout CE, Kim WT, et al. Cerebral arterial fenestrations. *Interv Neuroradiol.* 2014; 20: 261-274.
47. Hansen AG, Helvik AS, Nordgård S, et al. Incidental findings in MRI of the paranasal sinuses in adults: A population-based study (HUNT MRI). *BMC Ear Nose Throat Disord.* 2014;14:13-
48. Hansen AG, Stovner LJ, Hagen K, Helvik AS, Thorstensen WM, Nordgård S, Bugten V, Eggesbø HB. Paranasal sinus opacification in headache sufferers: A population-based imaging study (the HUNT study-MRI). *Cephalalgia.* in press.
49. Nazri M, Bux SI, Tengku-Kamalden TF, Ng KH, Sun Z. Incidental detection of sinus mucosal abnormalities on CT and MRI imaging of the head. *Quant Imaging Med Surg.* 2013;3:82-88.
50. Evans RW, Peres MF. Headaches and pineal cysts. *Headache.* 2010;50:666-668.
51. Seifert CL, Woeller A, Valet M, et al. Headaches and pineal cyst: A case-control study. *Headache.* 2008;48:448-452.
52. Al-Holou WN, Terman SW, Kilburg C, et al. Prevalence and natural history of pineal cysts in adults. *J Neurosurg.* 2011;115:1106-1114.
53. Nevins EJ, Das K, Bhojak M, et al. Incidental pineal cysts: Is surveillance necessary? *World Neurosurg.* 2016;90:96-102.
54. McNeill KA. Epidemiology of brain tumors. *Neurol Clin.* 2016;34:981-998.
55. Kreitschmann-Andermahr I, Siegel S, Weber Carneiro R, Maubach JM, Harbeck B, Brabant G. Headache and pituitary disease: A systematic review. *Clin Endocrinol (Oxf).* 2013;79:760-769.
56. Edvardsson B. Symptomatic cluster headache: A review of 63 cases. *Springerplus.* 2014;3:64.
57. Levy MJ, Matharu MS, Meeran K, et al. The clinical characteristics of headache in patients with pituitary tumours. *Brain.* 2005;128:1921-1930.
58. Snyder PJ, Incidentally discovered sellar masses (pituitary incidentalomas). In UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed January 22, 2017.
59. Okuda DT, Mowry EM, Beheshtian A, et al. Incidental MRI anomalies suggestive of multiple sclerosis: The radiologically isolated syndrome. *Neurology.* 2009;72:800-805.
60. Granberg T, Martola J, Aspelin P, et al. Radiologically isolated syndrome: An uncommon finding at a university clinic in a high-prevalence region for multiple sclerosis. *BMJ Open.* 2013; 3:e003531.
61. Forslin Y, Granberg T, Jumah AA, et al. Incidence of radiologically isolated syndrome: A population-based study. *AJNR Am J Neuroradiol.* 2016;37:1017-1022.
62. Labiano-Fontcuberta A, Benito-León J. Radiologically isolated syndrome: An update on a rare entity. *Mult Scler.* 2016;22:1514-1521.
63. Liu S, Kullnat J, Bourdette D, et al. Prevalence of brain magnetic resonance imaging meeting Barkhof and McDonald criteria for dissemination in space among headache patients. *Mult Scler.* 2013; 19:1101-1105.
64. Larkin S, Karavitaki N, Ansorge O. Rathke's cleft cyst. *Handb Clin Neurol.* 2014;124:255-269.
65. Aho CJ, Liu C, Zelman V, Couldwell WT, Weiss MH. Surgical outcomes in 118 patients with Rathke cleft cysts. *J Neurosurg.* 2005; Feb102:189-193.
66. Hoang S, Choudhri O, Edwards M, Guzman R. Vein of Galen malformation. *Neurosurg Focus.* 2009;27:E8.
67. Matthies C, Samii M. Management of 1000 vestibular schwannomas (acoustic neuromas): Clinical presentation. *Neurosurgery.* 1997;40:1-9.
68. Park JK, Vernick DM, Ramakrishna N, Vestibular schwannoma (acoustic neuroma). In UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed January 19, 2017.
69. Carlson ML, Tveiten ØV, Driscoll CL, et al. Risk factors and analysis of long-term headache in

sporadic vestibular schwannoma: A multicenter cross-sectional study. *J Neurosurg.* 2015;123:1276-1286.

70. Suwanwela N, Phanthumchinda K, Kaoropthum S. Headache in brain tumor: A cross-sectional study. *Headache.* 1994;34:435-438.
71. Groeschel S, Chong WK, Surtees R, Hanefeld F. Virchow-Robin spaces on magnetic resonance images: Normative data, their dilatation, and a review of the literature. *Neuroradiology.* 2006;48: 745-754.
72. Husøy AK, Indergaard MK, Honningsvåg LM, et al. Perivascular spaces and headache: A population-based imaging study (HUNT-MRI). *Cephalalgia.* 2016;36:232-339.
73. Evans RW. Diagnostic testing for migraine and other primary headaches. *Neurol Clin.* 2009; 27: 393-415.
74. 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.