Expert Opinions

Incidental Findings and Normal Anatomical Variants on Brain MRI in Children for Primary Headaches

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When MRI scans of the brain are obtained for evaluation of primary headaches in children, incidental findings and anatomical variants are commonly present. After a review of the prevalence, 11 types are presented.

Key words: MRI of the brain, incidental findings, anatomical variants, headache, pediatric headache, pituitary enlargement, benign enlargement of subarachnoid spaces in infancy, periatrial cyst, periventricular leukomalacia, heterotopia, cortical dysplasia

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Headache is a relatively common symptom in children. In 1962, the landmark epidemiologic survey published by Bille surveyed 9,000 school children, finding that one-third of 7-year-old children and one-half of 15-year-old children reported having at least one headache. Prepubertal boys are more affected than girls; however, after puberty, headaches become more common in girls.¹ The prevalence of migraine among children and adolescents is in the range of 7.7-9.1% more prevalent in girls than boys.² Although most pediatric patients do not have a serious underlying cause of their headaches, neuroimaging can be a valuable diagnostic tool to evaluate for

secondary headache. Not uncommonly, imaging will detect an incidental finding or anatomical variant, which may cause concern for the patient and parents. The topic of incidental findings in adults is covered in a recent "Expert Opinion."³

CASE HISTORY

This is a 16-year-old female who presented with headaches increasing in frequency and intensity over a 5-month period. She described a bioccipital sharp pain with an intensity of 8/10 associated with nausea, vomiting, blurred vision, light and noise sensitivity. She took over the counter analgesics with a continued duration of hours to a full day. The headaches would awaken her from sleep. She had no decrease with amitriptyline and a mild decrease in frequency with topiramate.

Due to several concerning features of worsening pattern, occipital location, nighttime awakening, and nonresponsiveness to medications, further imaging was ordered. MRI of the brain with and without contrast was obtained, shown in Figure 1

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Fig. 1.—Diffuse enhancement and thickening of the pituitary stalk extending to the upper margin of the pituitary gland.

(sagittal T1 with contrast, coronal T1 with contrast). Initial differential diagnosis included lymphocytic hypophysitis, eosinophilic granulomatosis, lymphoma, leukemia, and cell tumor. Repeat imaging over 1 year remained unchanged. Based on age of presentation and stability of the imaging over time, this likely represents physiologic pituitary enlargement.

Questions.—When should imaging be performed in children with headaches? How often and which incidental findings in children with headaches and migraine? In alphabetical order, what are some incidental findings and anatomical variants, which may be encountered?

EXPERT OPINION

When Should Imaging Be Obtained in a Pediatric Patient With Headaches?—Practice parameters for the evaluation of children and adolescents with recurrent headaches, published in 2002, recommend that diagnostic neuroimaging be considered for children with an abnormal neurologic examination or other physical findings that suggest CNS disease. Variables that predict the presence of a space-occupying lesion included (1) headache of <1-month duration; (2) absence of family history of migraine; (3) abnormal neurologic findings on examination; (4) gait abnormalities; and (5) occurrence of seizures.⁴ These recommendations agreed with the previous practice parameters for the

evaluation of headache in adults, published in 1994 and 2000, but emphasized that obtaining a neuroimaging study on a routine basis is not indicated for children with recurrent headache and a normal neurologic examination. Most children with recurrent headaches have primary headaches of benign etiology. Children with non-migrainous headache episodes lasting more than 6 months and a normal neurologic exam have a low baseline risk for brain tumor of 0.01%. Close clinical follow-up without imaging is the most cost-effective strategy.⁵

As in our case, children with occipital headache are more likely to undergo neuroimaging because there is concern that occipital headaches are rare and suggest serious intracranial pathology. Two recent studies find that occipital headaches alone without focal neurological findings are not a red flag for neuroimaging. In a retrospective outpatient study of 308 patients ages 18 or younger, headaches were occipital alone in 7% and occipital and other locations in 14%. Occipital pain alone or along with other locations was not associated with clinically significant imaging findings.⁶ In a retrospective study of 314 children aged 5-18 years seen in the emergency department, 39 had occipital headaches. There was no difference in final diagnosis between the occipital and nonoccipital groups and no patients had brain tumors.

There may also be concern as in our case about nighttime or awakening pain as a red flag for a

possible brain tumor. However, this is commonly reported in pediatric migraine. In a study of 160 children, awakening pain was reported by 42%.⁷

How Common Are Incidental Findings in Pediatric Patients with Headaches?—Incidental findings are defined as image findings that are not likely the cause of the patient's headaches. Incidental findings are commonly present in children on brain MRI scans,⁸ although the reported rates have varied, with 9% in a Japanese study,⁹ 21% in an American study,¹⁰ and 23% in a Malawian study.¹¹

In a retrospective study of 241 children and adolescents who had MRI or CT imaging for headache (90% MRIs), 19.1% were found to have 50 benign abnormalities including the following: sinus disease, 13; Chiari I malformation, 11; nonspecific white matter abnormalities (WMA), 7; venous angiomas, 5; arachnoid cysts, 5; enlarged Virchow-Robin spaces (VRS), 4; pineal cysts, 2; mega cisterna magna, 1; fenestration of the proximal basilar artery, 1; and periventricular leukomalacia, 1.¹² In another retrospective study of 324 children who had MRI scans for headaches, 8.9% had incidental brain findings.¹³ A meta-analysis of 17 imaging studies for pediatric headache had a similar prevalence of incidental findings.¹⁴

In Alphabetical Order, What Are Some of the Incidental Findings and Anatomical Variants That May Be Encountered?—Brain Tumors.—The relationship between brain tumors and headache is difficult to define, and is often thought of as an incidental finding unless there are associated image findings of edema, hydrocephalus, hemorrhage, or clinical findings of increased intracranial pressure. Brain tumor is less common in children than adults, despite being the largest cause of solid tumors in children. Based upon data from the Central Brain Tumor Registry of the US, the estimated incidence of primary non-malignant and malignant CNS tumors is 5.4 cases per 100,000 person-years for children and adolescents <19 years of age.¹⁵ Posterior fossa tumors are estimated to be 50-55% of all brain tumors in children, and they are much more common in children than in adults. There is a different distribution seen based on age, with children <3 years of age being more common supratentorially, children 4-10 years old more common infratentorially, and in children >10 years old equal in location.¹⁶

Benign Enlargement of Subarachnoid Spaces in Infancy (BESSI).-Macrocephaly (head circumference >95%) typically presents at 3-4 months, but can be noted at birth, and spontaneously resolves by 2-3 vears of age.¹⁷ Incidence of BESSI is not well documented. There can be a family history of macrocephaly. Radiologically, there is widening of the bifrontal and anterior interhemispheric CSF spaces with normal ventricles. Imaging is usually obtained for macrocephaly seen on exam and there is typically no association with headache, but children with BESSI are at increased risk for subdural hemorrhage with minor trauma from tearing of bridging veins, which can present as headache. Further workup recommended includes monitoring head circumference and development. Repeat imaging is only recommended in cases of enlarged ventricles, head circumference not parallel to the curve, abnormal neurological exam, or signs of increased intracranial pressure.¹⁸

Cortical Dysplasia.—Focal cortical dysplasia is a congenital disorder of failure of proper neuronal migration. Radiologically, cortical dysplasia can appear to have cortical thickening, blurring of white matter–gray matter junction with abnormal architecture of subcortical layer. MRI can also show segmental or lobar atrophy with or without hypoplasia of regional white matter.¹⁹ Temporal or frontal lobes most common location. There is no known association with headaches and further workup is not recommended. While focal cortical dysplasia is associated with increased risk of seizure, routine EEG is not recommended.

Cysts (*Colloid, Mucosal, Arachnoid, Pineal, Rathke*).—Pituitary enlargement is the most common incidental finding and Rathke's cleft cysts account for the least common finding among children. For further discussion on specific cysts and their incidence in children, associated imaging appearance, headache significance, and surveillance recommendations, please reference Table 1.²⁰⁻²⁷

Developmental Venous Anomalies (DVAs).—DVAs, also known as venous angiomas, have been reported in 0.3-2.1% pf pediatric patients

Cyst Type	Incidence	Description	Location(s)	Imaging Characteristics (MRI)	Headache Significance	Further Work up	Reimaging (MRI) Recommendations
Arachnoid	1-3.2% ¹²	Congenital or acquired, nonneoplastic, fluid-filled cysts that occur on the arachnoid membrane	Supratentorial- anterior middle fossa, perisellar cisterns, SA spaces over convexities ²⁷	Extraaxial mass, T1 hypointense, T2 hyperintense (same signal intensity as CSF in all sequences), hypointense on DWI ²⁷	Headache is most common symptom, but cyst often incidental ²⁵	If focal neurologic or ICP symptom/ signs, then NSG referral ²⁵	If focal neurologic or ICP symptoms/signs develop ²⁵
			Infratentorial- retrocerebellar cistern, CPA cistern, quadrigeminal plate cistern ²⁷				
Colloid	0.5-1.0% ²⁶	Nonneoplastic epithelial lined cyst	Anterior portion of the third ventricle near the foramen of Monro ²⁷	T1 isodense to hyperintense, T2 f hypointense, hyperintense, (T1 intensity proportional to proteinacous	Positional headache with or without ICP symptoms/signs ²⁶	If hydrocephalus, then urgent NSG referral ²⁶	Worsening headache especially with ICP symptoms/signs ²⁶
Mucous Retentio:	Incidence not well n known in pediatric one study reports 1.4-9.6% in the general noonlation ²²	Small encapsulated s; globules of mucous or serous material	Frontal, ethmoid, or sphenoid sinuses ²¹	Thypointense with gadolinium, enhanc- ing rim, T2 hyperintense ²¹	Frontal headaches ²¹	If expansive, ENT referral due to risk of bone erosion ²¹	None ²¹
Pineal Gland	0.8-2.1 ¹²	Nonneoplastic proteinaceous fluid filled cyst	Pineal gland	T1 isointense to slight hyperintense, T2 hyperintense. Many have ring enchancement due to surrounding two limbs of internal cerebral veins ²⁷	Headaches are coincidental, unless secondary to hydrocephalus. If large enough, can cause gaze palsy and Parinaud's syndrome ²⁰	NSG referral if >1 cm in maximal dimension ²⁰	Growth in childhood, then involute during adulthood. Repeat MRI in 1 year in assymptomatic children ²⁰

Table 1.—Cysts and Headache

Reimaging (MRI) Recommendations	If diameter < 10 mm, obtain yearly MR1 ²² If diameter > 10 mm or extension, also recommend yearly visual field testing ²² If > 10 mm or if suprasellar, surgical intervention may be indicated ²²
Further Work up	If visual deficits, referral to NSG If visual deficits, referral to optho referral to optho although without visual deficits can be managed medically ²⁴ Risk of pituitary apoplexy and aseptic meningitis ²
Headache Significance	Most commonly asymptomatic. Headaches can indicate symptomatic especially if also with visual field deficits and deficits and deficits and deficits and deficits and deficits and diabetes insipidus) ²
Imaging Characteristics (MRI)	Well circumscribed, little to no contrast enchancement, variable T1 and T2 intensities due to cystic contents ²² cystic contents ²² pediatrics, small autopsy study showed <2 mm ²²
Location(s)	Most commonly pars vintermedia-between anterior and posterior pituitary, sellar and suprasellar ²²
Description	Nonneoplastic cystic lesion containing mucoid material, arises in embryologic remnants of Rathke's pouch
Incidence	Incidence not well known in pediatrics; one study reports 1.2% of < 15 years have incidental pituitary cysts ²²
Cyst Type	Rathke's Cleft

CPA = cerebellopontine angle; DWI = diffusion weighted imaging; ENT = otolaryngology; ICP = intracranial pressure; NSG = neurosurgery; SA = subarachnoid.

Headache

Table 1.—Continued

imaged,^{5,12,28,29} which is similar rate of 2.5% reported in a large postmortem study of 4,069 serial cases.³⁰ DVAs are congenital anomalies of intracranial venous drainage characterized by the "caput medusae sign" of veins draining into a single larger collecting vein, which in turn drains into either a dural sinus or into a deep ependymal vein. Histologically, DVAs consist of thickened veins with normal feeding arteries and capillaries.³¹ DVAs usually are an isolated lesion (75%) and are found most commonly in the frontoparietal region usually draining towards the frontal horn of the lateral ventricle (36-64%) or the cerebellar hemisphere draining toward the fourth (14-27%).³² Review of susceptibility ventricle weighted sequences is recommended to evaluate for an associated cavernous hemangioma, which can occur in up to 33% of patients with DVAs.^{33,34} Although usually DVAs are considered asymptomatic and do not require surgical intervention or further monitoring, DVAs associated with cavernous angiomas or other vascular malformations have significantly higher hemorrhage rates and these patients should be referred for neurosurgical consultation for consideration of surgical resection.³⁵ There is also an association of DVA with cortical dysplasia,³⁶ which as mentioned above can increase the risk of seizure.

Grav Matter Heterotopias.-Grav matter heterotopia is a congenital disorder of failure of proper neuronal migration that typically presents with seizures and developmental delay. Radiologically, there are two distinct types are seen: diffuse and nodular. Heterotopias consist of gray matter located outside the normal distribution, typically with indistinct margins and with no enhancement. There is no known headache association. Etiology of gray matter heterotopias is often multi-factorial but can be associated with genetic disorders including tuberous sclerosis (TS). The subependymal tubers seen in TS can be differentiated from heterotopias, as tubers will enhance on contrasted MRI.37 Children with subependymal heterotopias and tubers should be monitored and evaluated for seizures.

Mega Cisterna Magna.—This finding is as its name suggests an enlarged cisterna magna, which is an enlarged subarachnoid space in the inferior and posterior portions of the posterior fossa with a

normal appearing cerebellar hemispheres, vermis, and fourth ventricle. Septa may be seen within a mega cisterna magna, which are thought to be Blake pouch vestigial remnants. This finding is seen incidentally in 0.4% of pediatric patients.¹² If suspected on CT imaging, MRI is recommended to further evaluate. Midsagittal views show a cisterna magna that measures >10 mm. Additional CSF flow studies with MRI can help assess for communication between a cystic mass and the subarachnoid space. Mega cisterna magna is considered a benign, asymptomatic finding and does not require any further follow-up imaging or intervention. However, careful attention is needed to evaluate that this finding is not confused for an arachnoid cyst, epidermoid cyst (heterogeneous/dirty signal on FLAIR and restricted diffusion), cerebellar atrophy, congenital cerebellar hypoplasia, Dandy-Walker malformation (abnormal vermis), Blake's pouch cyst (associated hydrocephalus), or oncologic process such as a pilocytic astrocytoma (posterior and predominantly cystic).

Periventricular Leukomalacia (PVL).-These white matter lesions, which result from hypoxia or ischemia in the prenatal or perinatal period, typically present with cerebral palsy, developmental delay, or vision problems. There is no known association with headache. Mild PVL may only have subtle findings of hypertonia, early handedness (before age 2), or motor developmental delays. Rates of PVL occur in 1-2 of 1,000 births (higher in preterm births).³⁸ In the acute period of injury, MRI shows T1 hyperintensity within areas of T2 hyperintensity. Remote from the injury, MRI will demonstrate ventriculomegaly related to tissue volume loss with irregular margins of the lateral ventricles, loss of periventricular white matter with increased T2 signal, and thinning of the corpus callosum. Not all PVL may be symptomatic, and with the increasing use of FLAIR weighted images, it is possible that non-specific white matter changes, signal variations, and even PVL may be underreported or interchangeably classified. Isolated PVL without a history of intraventricular hemorrhage is associated with the development of cerebral palsy, most commonly symmetrical spastic diplegic type.³⁹ If PVL is a newly discovered finding, evaluation by physical therapy or occupational therapy is recommended, but no further workup or imaging is recommended. Physiologic Pituitary Enlargement.-Incidental pituitary imaging findings are so common that the term "pituitary incidentaloma" is used in the literature. Pituitary enlargement is a common referral to pediatric neurosurgery especially if it associated with headache or endocrine signs or symptoms. Many studies have documented physiologic pituitary hypertrophy in early to mid-teenage years in mostly girls. In patients with headache and visual disturbances along with galactorrhea, pituitary adenomas are considered. Although most adenomas are detected on a nonenhanced MRI, microadenomas may become visible only after contrast injection as they appear dark due to lack of contrast uptake compared to normal pituitary tissue. To demonstrate this finding, MRI is best done within 1 minute of contrast injection, and if delayed (20 min after contrast injection), the tumor may enhance.⁴⁰

Screening evaluation of pituitary enlargement includes TSH, free T4, T3, cortisol, insulin-like growth factor 1, prolactin, and in postmenarchial girls, beta human chorionic gonadotropin. Surgery through a transsphenoidal surgical approach is offered for secreting adenomas. There are studies where surgery showed improvement in headaches; however, it is difficult to speculate on the cause of headache in nonfunctioning adenomas.⁴¹

VRS and Enlarged Perivascular Spaces.—VRS are normally sized perivascular spaces of interstitial fluid that surround intracranial blood vessels that can be appreciated on 1.5 Tesla MRI. Radiologically, VRS are smoothly demarcated fluid-filled cysts, which follow CSF attenuation. They are most commonly found in the anterior commissure, vertex, basal ganglia, and midbrain.

Enlarged perivascular spaces (typically < 5 mm) can be still be a normal variant that develops with age as the brain atrophies. However, severely enlarged perivascular spaces can develop early in the setting of metabolic/genetic, vascular, inflammatory, neoplastic etiologies, and mild traumatic brain injury. Most cases of enlarged perivascular spaces are asymptomatic, but can be seen more frequently in migraineurs.⁴²

WMA of Unknown Significance.--Nonspecific WMA are commonly found in 4-5% of all pediatric MRIs.⁴³ They appear as small hyperintense foci on T2-weighted sequences. The CAMERA-1 study (Cerebral Abnormalities in Migraine, an Epidemiological Risk Analysis) reported adult migraineurs have a higher prevalence of deep white matter hyperintensities, infratentorial hyperintensities, and posterior circulation territory infarct-like lesions.⁴⁴ The CAMERA-2 study, which is a follow-up from the CAMERA-1 study, reassesses the same adult patients 9 years later, looking at progression of their MRI abnormalities, finding that women with migraine had a higher incidence of deep white matter hyperintensities but did not have significantly higher progression of other MRI-measured brain changes. There was no association of migraine with progression of any MRI-measured brain lesions in men.⁴⁵ Uggetti et al has questioned the increased prevalence of WMA in younger migraine populations. In migraine, WMA are typically supratentorial with no associated increased risk of brainstem or cerebellar lesions.⁴⁶ In contrast, multiple sclerosis (MS) lesions, there is preferential involvement of the subcortical U-fibers, the corpus callosum, temporal lobes, and the brainstem/cerebellum. MS periventricular lesions are ovoid and perpendicular to lateral ventricles.⁴⁷⁻⁴⁹ For lesions meeting the Okuda criteria of radiologically isolated syndrome, follow-up imaging should be considered on a caseby-case basis.⁵⁰

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