

Secondary Headache



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Primary headache disorders are benign and the most commonly encountered headaches. Secondary headache is a headache syndrome which has been precipitated by a non-benign pathology. There is robust clinical data supporting the classification of primary headaches. However much of the classification of secondary headaches has yet to be adequately validated.

The International Classification of Headache Disorders (ICHD) divides the primary headaches into four sections: Migraine, Tension-Type Headache, the Trigeminal Autonomic Cephalalgias (cluster headache and related disorders), and a group of Other Primary Headaches consisting largely of a group of paroxysmal headache disorders. There is no readily available diagnostic marker for pain, let alone subtypes of pain. Structural imaging, computerized tomography (CT) and magnetic resonance imaging (MRI), have no diagnostic value in primary headache. Accurate diagnosis and treatment remains clinical. There is increasing evidence that individuals who experience headaches have a genetic predisposition and that headache is principally a disorder of central nervous system mechanisms.¹

What are the most reliable indicators of secondary headache? Which patients should be investigated and how? Imaging studies in headache are compounded by inconsistency. Not all have used the ICHD for primary headaches, thus categorization of 'typical' and 'atypical' headache remains contentious. MRI studies reveal detail which cannot be visualised on CT. The question is whether the detail is pertinent to address if the headache is caused by the abnormality. Finally, there is the matter of uniform practice. What abnormality on imaging is considered to be benign? What should be kept under surveillance and what warrants intervention and when?

Imaging in "Normals"

It is first informative to look at imaging asymptomatic healthy individuals. A total of 2,536 healthy male German Air Force recruits underwent MRI. Abnormalities were found in 6.55% of scans; all were clinically silent. Of the total cohort 0.55% had significant lesions warranting surveillance or intervention (Table 1).² Examination of 1000 MRI brain scans on healthy paid volunteers revealed 1.8% benign findings to which the patients' clinicians were made aware.

Table 1. Imaging in Healthy Individuals

Study	Patients N	Mean age	Type of Scan	Total % abnormal scans	Insignificant abnormalities		Significant* abnormalities	
					%	Nature	%	Nature
(2) Prospective German Airforce Recruits	2,536	20.5	MRI	6.55	6.0	Colloid cyst 3rd ventricle, pituitary adenoma, arachnoid and other cystic, vascular lesions, cortical atrophy, cerebellar dysplasia, hygroma, chiari I, cervical disc prolapse.	0.55	Arteriovenous malformations, cavernomas, primary brain tumours and demyelinating disease
(3) Retrospective Paid research volunteers	1000	30.6	MRI	18	15.1	Sinusitis, age related changes, T2 hyperintensities, mastoid/petrous fluid	1.1 (urgent referral) 1.8 (routine referral)	Arachnoid cyst, cavernous angioma, oligodendroglioma, pilocytic astrocytoma, aneurysm, low grade glioma, Benign cysts, prominent temporal horns, old traumatic changes, old lacunes, demyelinating lesion, scalp cystic lesions
(4) Population-based Rotterdam Study	2000	63.3	MRI	10.6	10.6	Asymptomatic brain infarcts	1.8	Aneurysm
					<0.1	Subdural haematoma	<0.1	Metastatic disease
					<0.1	Dermoid cyst Fibrous dysplasia	0.5	Major vessel stenosis
					0.4	Cavernous angioma	1.6	Primary benign tumours
					1.1	Arachnoid cyst		
0.9	Chiari I							

* Significant = warranting surveillance or intervention

Abnormalities warranting further attention were found in 1.1% of scans.³ A European population-based study of 2000 individuals found 3.5% significant abnormalities on imaging. The higher prevalence was attributed to the scanning protocols used.⁴ Aneurysms comprised the largest group of incidental abnormalities at 1.8%, consistent with autopsy and angiographic data. Only one primary malignant brain tumour and one metastatic disease was found. Imaging of 3,672 individuals over 65 years of age showed significant abnormalities in 1.74%.⁵

Imaging patients with headache

The most common headaches are tension-type headache (prevalence range 30-80%)

and migraine (prevalence 12%). Patients with headache make up 4% of primary care attendees, 4% of emergency complaints and 30% of neurology outpatients. The majority of patients have a primary headache disorder.⁶

The American Academy of Neurology Practice Parameters advised that patients presenting with migraine headache, with or without typical visual aura and a normal neurological examination, have a very low risk of abnormality on imaging.⁷ Of 897 individuals imaged with MRI or CT 0.45% had an abnormality requiring surveillance or intervention (Table 2).

Of 1876 consecutive patients attending a headache clinic imaged with MRI or high resolution CT (mean age 38 years) incidental find-

ings considered benign were found in 0.75% of scans.⁸ Abnormalities considered to be significant were found in 1.2% of scans; 0.9% had a normal neurological examination (Table 1). The study also addressed the type of headache and proportion of lesions requiring surveillance or intervention in each headache group. Significant abnormalities were found in 0.8% of patients with tension-type headache, 0.4% with migraine, 5% with cluster headache and 3.7% in those in whom the clinical syndrome could not be clearly defined by the ICHD. Patients who had not responded to appropriate treatment and who had had CT also underwent MRI. Of a total of 199 scans two MRI scans were abnormal in patients with normal CT. One revealed a small meningioma

Table 2. Imaging in Headache Patients.

Study	Patients N	Type of Scan	Type of Headache	Insignificant abnormalities		Significant* abnormalities		Comments
				%	Nature	%	Nature	
(7) Retrospective	897	CT & MRI	Migraine w/ visual aura. Normal neurological examination.	–	–	0.4	Glioblastoma, Papilloma of the choroid plexus, other tumour**, AVM**.	** Presented with seizures.
	1825		Unspecified headache (no information about examination).			2.4	AVM, tumour, aneurysm, hydrocephalus.	
(8) Prospective	1876	CT MRI	Migraine TTH Cluster Indeterminate.	–	–	1.2 (0.9% if neurological examination normal)	Pituitary adenoma, large arachnoid cyst, meningioma, hydrocephalus, Chiari type I, ischaemic stroke, cavernous angioma, AVM, low-grade astrocytoma, brain stem glioma, colloid cyst and posterior fossa papilloma.	119 patients had CT (normal) & MRI. MRI in 2 – acoustic neuroma and small meningioma. Abnormal neurological examination – predictor of significant abnormal imaging 3 patients with normal imaging diagnoses with idiopathic intracranial hypertension from clinical examination.
	1432 580					0.8 0.4 5 3.7 (% of each headache type with significant imaging abnormalities)		
(26) Retrospective Normal neurological examination	373	CT (72.6% with contrast)	Migraine 76.1% TTH 23.1% Cluster 0.8% Referral criteria for headache: Increase severity, drug resistance, change in pattern, family history brain lesion.	3.5%	Old infarcts, atrophy, cavum vergae, hyperostosis frontalis, communicating hydrocephalus.	1	Low grade glioma, Osteoma, 5mm posterior communicating artery aneurysm.	In this paper - review of 6 studies of headache & CT – total 1,825 – 2% significant abnormalities.
(27) Prospective Normal neurological examination	306	MRI	Recurrent or chronic headache (>15 days/month).	44.1%	'Minor abnormalities.'	0.7	Pituitary macroadenoma and subdural hematoma.	Review of 12 studies of uncomplicated migraine and MRI in 771 patients – significant abnormality found in 0.58%. In 1036 'unspecified headache' significant abnormality in 2.1%.

AVM – Arteriovenous malformation

Table 3. Secondary Non-Traumatic Headache presenting to the Emergency Services

Study	No. of patients	% of total Emergency visits	Secondary Headache %	Primary Headache			
				Migraine	Tension-Type	Non-Specific	Other
(10) Prospective	558	0.85	13.7	22	11.1	17.6	3.4
(28) Retrospective	100	-	8	42	-	42	8
(29) Prospective	277	1.7	5	60	8	25	2

Table 4. Presentation of Brain Tumours (30)

Total Brain Tumours (N)	Primary	Secondary
Initial manifestation	%	%
Focal symptoms/ signs	58.8	55.9
Seizures	8.2	10.5
Headache	9.3	7.0
Headache + Focal	15.5	16.2
Seizures + Focal	2.1	4.7
Headache + Focal + seizures	0	1.2
Asymptomatic	6	4.7
At diagnosis		
Headache	33	31
Headache as first symptom	9.3	7
Headache as first and sole symptom at diagnosis	0	17
Longest duration of headache as isolated symptom	Not applicable	77 days

Most reliable indicators of Secondary Headache

- Sudden Onset Headache ('Thunderclap Headache')
- Age > 50 years old
- Additional neurological features
- Additional systemic features

and the other an acoustic neuroma.

The only variable associated with a higher probability of a pertinent intracranial abnormality was neurological examination. None of the following had predictive value: sex, age, duration of headache, intensity or worsening of headache and type of headache. Notably three patients with normal imaging were diagnosed with idiopathic intracranial hypertension based upon the clinical examination.

Table 2 gives a summary of further cohorts of patients with headache imaged with CT or MRI and confirms that ≤1% of patients presenting with typical migraine or tension-type headache will have an abnormality on imaging which warrants surveillance or intervention. Patients with headache which cannot clearly be classified or in whom neurological examination is abnormal have a higher probability of a significant abnormality on imaging at about 2-3%.

Secondary (non-traumatic) headache

Most secondary headache is identified through the emergency services. Only 0.1% presents through primary care⁹ (Table 3).

The most common reason for attendance to the emergency services with headache is for severity, recurrent headache and additional features.¹⁰ However neither severity nor response to drug treatment differentiate between primary and secondary headache. Headache associated with subarachnoid hemorrhage, venous sinus thrombosis, carotid

dissection and carbon-monoxide poisoning have all been reported to respond to sumatriptan.¹¹ Both recurrent headache and chronic headache do not seem to indicate a secondary pathology.^{8,10}

The most consistent indicators for secondary headache are sudden onset headache (thunderclap headache),^{10,12,13} age over 50 years^{11,14} and any neurological abnormality or additional systemic features.^{6,8,10} Clinically it is not possible to differentiate between primary and secondary thunderclap headache. Therefore all patients presenting with thunderclap headache should be investigated.

Headache and brain tumours

In a study of 183 patients with brain tumour, headache was the presenting complaint in 15%. Only in the metastatic group was headache the sole symptom at presentation. The longest duration of isolated headache before development of additional neurological symptoms was 11 weeks. The majority of patients with symptomatic brain tumour presented with focal neurology.

Findings were similar in a prospective study of 206 patients diagnosed with brain tumour. Fifty-five percent complained of new onset headache or change in pattern of existing headache.¹⁵ Eighty-five percent became pain free or markedly improved post-operatively; in 15.3% of this group headache appeared to be the sole presenting manifestation. By the time

of diagnosis 96% had already presented with other neurological symptoms or signs. 'Intracranial tumour headache' is currently defined by then ICHD by severity of pain, morning occurrence and association with nausea or vomiting. Only 5.1% of patients fulfilled these criteria. In half of the patients the features were consistent with those of episodic tension-type headache or migraine without aura (Table 4). Nausea has an 80% specificity for a diagnosis of migraine¹⁶ and can occur in up to 90% of migraine sufferers.¹⁷ Moreover, migraine attacks have shown a morning preponderance of onset.¹⁸ In this study a longstanding history of a primary headache disorder was an independent risk factor for developing headache associated with brain tumour.

This data is similar to data for other types of precipitated headache, which show that the clinical syndrome of the precipitated headache can be exactly the same as a primary headache syndrome and respond to treatments effective for that headache phenotype, irrelevant of precipitating pathology.^{19,21} Removal of the precipitant may result in improvement of the headache but this is not invariable.^{22,24}

Scanning for Reassurance

Proponents for imaging headache argue that the reassurance achieved by a normal scan has beneficial therapeutic value and is cost effective in reducing repeated attendance.⁸ One study has shown that the reassurance achieved by imaging was not maintained at one year. However, during this time patients scoring 11 or more on the Hospital Anxiety and Depression Scale had utilized health resources less.²⁵ Primary headache disorders can remain lifelong. Imaging may simply delay appropriate management of the headache disorder. Furthermore, the number of benign abnormalities on imaging is not insignificant. This can drive further unnecessary concern, or at worst unnecessary intervention.

Summary

Most patients who present with secondary headache do so through the emergency services. Isolated headache is a poor indicator of an underlying sinister brain pathology. The longer headache remains isolated the more likely it is to be benign. Patients with secondary headache are more likely to be aged 50 years and over, present with thunderclap onset headache or, have accompanying focal neurology or systemic ill-health. The multiple

'red-flags' for secondary headache are covered within these four most consistent indicators.

The clinical syndrome of the headache, severity and response to treatment are not reliable indicators of secondary headache. The majority of patients presenting with secondary headache have features of migraine or tension-type headache. Patients with new onset isolated headache with another primary headache syndrome or 'atypical' characteristics may warrant further investigation, for example new

onset cluster headache. Such headache disorders are much less common. Evidence to guide whether other headache phenotypes are more likely to be associated with a secondary precipitant will take longer to establish.

The risk of imaging for reassurance brings with it a problematic 'incidentaloma' rate. In patients with normal imaging reassurance may detract from the main issue of managing the considerable morbidity associated with the primary headache disorder. ♦

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