DIAGNOSTIC TESTS

Imaging in headache disorders

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SUMMARY

Patients with a suspected change in intracranial pressure or a trigeminal autonomic cephalgia require MRI.

The need for investigation for other headache disorders is guided by the clinical evaluation of the patient. Particular care should be taken to identify any 'red flags'.

Incidental findings on MRI occur in approximately 2% of patients. Patients with migraine have an increased rate of white matter lesions, but these are of uncertain clinical significance.

Introduction

Headache disorders are a leading cause of disability. Worldwide, migraine is the second leading cause of years lived with disability and, in Australia, it is among the top 20 reasons for consulting a GP.[1,2] While migraine is the most common disabling headache disorder, patients and clinicians are often concerned a headache could be a symptom of secondary pathology.

In a Norwegian population study, the one-year prevalence of secondary headaches was 2.14%. In 80% of these, the cause of the secondary headache could be diagnosed on the patient's history.[3]

In a UK tertiary referral headache service, 3655 consecutive patients were screened using 'red flags' to identify the need for imaging. Over a five-year period, 14.5% underwent imaging, with 11 patients having a significant finding. This represents 2.1% of patients scanned or 0.3% of the clinic population.[4]

There are several evidence-based guidelines that recommend that imaging of patients with headaches should not be routine. The need for imaging should be guided by clinical evaluation.[5-7]

Clinical evaluation

A thorough clinical assessment is essential for evaluating a patient who presents with headache and for determining the need for imaging. The key features of a headache history can be summarised by 'the 5Ps':

- patient
- pattern
- phenotype
- precipitants
- pharmacology.[8]

A thorough headache history, considering potential red flags (Table 1)[8] and 'green flags' (Table 2),[9] coupled with a detailed neurological examination is required. This not only determines the need for imaging, but also guides which imaging modality to use.

The recognition of red flags is useful for identifying which patients need further evaluation, however the specific differential diagnosis should be considered. This guides the choice of investigation and its urgency. For example, a patient with suspected stroke or meningitis requires urgent evaluation, while a patient with a recent change in the pattern of their headache is likely to be suitable for outpatient evaluation.

Green flags are reassuring features in a headache history (Table 2). They suggest a secondary cause of headache is unlikely. The green flags were determined by an expert group of the International Headache Society,[9] but have not been validated in a prospective study.

Patient

When deciding on the need for investigation, patient factors such as age and general health are the most critical consideration. A patient with new headaches late in life, or in the setting of malignancy or immunosuppression, always requires further evaluation, regardless of other factors. The presence of neurological or systemic signs in relation to the headache also requires further evaluation. Conversely, the presence of a strong family history of similar headaches is a reassuring factor.

Pattern

The temporal pattern of a patient's headache can help distinguish primary and secondary causes. A headache that has been present and unchanged from childhood, or is consistently related to menstruation, is less likely to have a secondary cause.[9] Conversely, a recent onset or new pattern is suspicious for a secondary cause of headache. The timing of the change in pattern can give a clue as to the cause, such as in the case of medication-overuse headache.

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Table 1 **The SNOOP4 list of 'red flags' for secondary headaches**[8]

	Mnemonic	Examples of red flags	Possible secondary headache
S	Systemic symptoms	Fever, weight loss	Meningitis, encephalitis, giant cell arteritis
	Secondary risk factor	Malignancy, immunosuppression	Metastasis, leptomeningeal carcinomatosis
N	Neurological deficit	Focal neurological sign, altered conscious state	Stroke, space-occupying lesion, hydrocephalus
O	Onset	Thunderclap, abrupt onset	Includes subarachnoid haemorrhage, pituitary apoplexy, cerebral venous sinus thrombosis
O	Older age	New or progressive headache (>50 years)	Mass lesion, giant cell arteritis
P4	Positional	Changes with change in posture	Intracranial hypotension or hypertension
	Pattern change	Change in character from baseline	Mass lesion
	Precipitated by	Valsalva, coughing, sneezing	Posterior fossa lesion
	Papilloedema	Visual obscuration	Idiopathic intracranial hypertension

Table 2 **Potential 'green flags' for primary headaches**[9]

Green flag	Rationale
The current headache was present during childhood	Secondary headaches are uncommon in childhood and common secondary causes in childhood (viral, post-trauma) do not usually persist.
The headache is temporally related to the menstrual cycle	Menstrually related migraine is common, and the probability of a migraine during the first three days of the menstrual cycle is elevated.
The patient has headache-free days	Most primary headache disorders are intermittent, whereas secondary causes (excepting brain tumours) are less commonly so, and secondary causes are less commonly associated with an identifiable trigger.
Close family members have the same headache type	Migraine and cluster headache can be inherited, and so the presence of a family history is supportive of the diagnosis.

Phenotype

The characteristics of a headache in an individual are called the phenotype. Accurate evaluation of the phenotype is key to determining the headache disorder. In the setting of an established, recurrent phenotype, the presence of a new phenotype requires increased clinical vigilance. However, the presence of a phenotype with features of a primary headache disorder, such as tension-type headache or migraine, should not provide false reassurance if there are red flags. For example, in one study of patients who were found to have primary or metastatic brain tumours, 77% presented with headaches phenotypically in keeping with tension-type headache.[10] Some phenotypes always require further evaluation. These include the 'thunderclap' headache and trigeminal autonomic cephalgias, such as cluster headache.

Precipitating factors

The relationship of the headache to precipitating or provoking factors can provide a further clue to the underlying aetiology. A trigger, for example alcohol, may suggest a primary headache disorder such as migraine or cluster headache, whereas eating tyramine-containing food while taking a monoamine oxidase inhibitor suggests a secondary cause. Precipitating factors such as the valsalva manoeuvre or a change with posture are concerning because they may be due to posterior fossa pathology or raised intracranial pressure. Headaches can occur solely in 'task-specific' settings, such as exertion, intercourse or sleep, and the clinician should be alert to these factors in the patient's history. Finally, new headaches that are 'precipitated' in the setting of pregnancy, postpartum, or ischaemic heart disease (cardiac cephalgia) may be suspicious for a secondary cause, and require specific consideration.

Pharmacology

Prescription and non-prescription medicines may precipitate or perpetuate headaches. As such, a detailed history noting the timing of new drugs and the pattern of headaches is required. The overuse of acute analgesia is a critical issue to be addressed in patients with a primary headache disorder. Medication-overuse headache may occur in over 70% of patients with a chronic daily headache.[11] Patients who regularly use opioid or triptan analgesia for more than 10 days/month or simple analgesia for more than 15 days/month are at risk of increased neuronal hyperexcitability, peripheral and central sensitisation, and further potentiation of their headaches.[11]

Headache may also be an adverse reaction to a prescribed drug. The product information of many medicines lists headache as a possible adverse effect. Careful attention should therefore be paid to the temporal relationship when evaluating the relationship between a new drug and headaches. There are several classes of drugs that are well known to precipitate headaches. These include tacrolimus, interferon-beta, nitric oxide donors, phosphodiesterase inhibitors, some antidepressants and ciclosporin.[12] Other drugs such as tetracyclines and vitamin A analogues may raise intracranial pressure, increasing the risk of idiopathic intracranial hypertension.[13]

Imaging of primary headaches

If imaging is indicated, MRI provides the most useful information. However, incidental findings are common and often result in patient anxiety, referral, and more imaging. Incidental findings on MRI occur in 2% of the general population.[14] These findings include neoplasia in 0.7%, aneurysm in 0.35%, arachnoid cysts in 0.5%, Chiari I malformations in 0.24% and demyelination in 0.06%.[14]

In patients without red flags, there is not an absolute need for imaging in every patient. The decision to proceed to imaging should be made with consideration of the possibility of incidental findings and the overall clinical picture.

In selected scenarios, CT may be considered, depending on the question to be addressed by the imaging. It may be adequate at identifying subdural or epidural haematoma, skull fracture, sinus infection or subarachnoid haemorrhage (depending on the timing of the scan following the index event).

Migraine

Migraine, as the most common disabling primary headache disorder, is frequently investigated to exclude secondary pathology. In population studies, women with migraine are at an increased risk of white matter lesions (odds ratio 2.1, 95% CI 1.0–4.1) and hyperintense lesions in the brainstem (4.4% vs 0.7%).[15] These findings are more common in patients with migraine aura, longer disease duration and higher attack frequency.[15] The clinical significance of these lesions is still a matter of ongoing research, however they are not believed to be associated with cognitive changes.[16,17] They can generally be differentiated from demyelination by an experienced reviewer, however serial imaging may be required.

Trigeminal autonomic cephalgias

The trigeminal autonomic cephalgias are a group of primary headache disorders characterised by unilateral (side-locked) headaches and ipsilateral cranial autonomic symptoms. All patients with a trigeminal autonomic cephalgia are required to have MRI primarily to exclude pathology in the pituitary region.

Ideally, the MRI would be of the brain and pituitary region, however it is not uncommon that just the brain is imaged. A review has now recommended that further dedicated pituitary imaging is only required if there are atypical features (older age, prolonged duration, higher frequency of attacks, bilateral attacks (rare, and should precipitate specialist review) or the absence of autonomic symptoms), pituitary-related symptoms, an abnormal examination or a poor response to treatment.[18,19] Among 376 patients with cluster headache, the rate of pituitary adenomas was similar to the rate in the general population. Only patients with suggestive symptoms therefore require an additional MRI of the pituitary.[19]

Other primary headache disorders

Several primary headache disorders specifically require imaging to evaluate the patient for a possible secondary cause. Primary headache associated with sexual activity should be considered as attributed to reversible cerebral vasoconstriction syndrome until proven otherwise by angiographic study.[20] Similarly, the diagnosis of primary exertional headache first requires evaluation for other causes of thunderclap headache.[20] Primary cough headache should be evaluated with MRI particularly to check for posterior fossa pathology or structural malformations such as the Chiari I malformation.[20,21]

Imaging of secondary headaches

When investigating for a secondary headache, the clinical situation needs to be considered.

Thunderclap headache

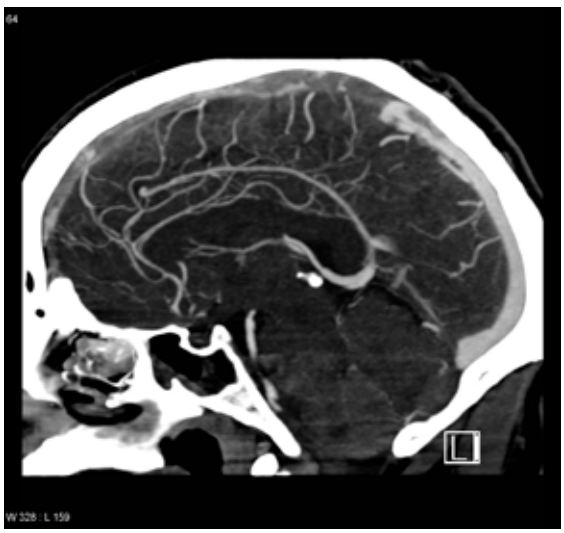
Thunderclap headaches are sudden and severe. They are often due to cerebrovascular disorders, such as

subarachnoid haemorrhage (see Box[22-24] and Fig. 1[25]). A non-contrast CT is frequently ordered for a patient presenting with a thunderclap headache. If performed within six hours of onset, CT has a sensitivity of 98.7% (CI 97.1–99.4%),[26] however this drops considerably after six hours.[27] A negative CT scan therefore may be falsely reassuring for ruling out subarachnoid haemorrhage, depending on the timing. CT is also likely to miss differential diagnoses that may be clinically relevant, including cerebral venous sinus thrombosis (see Fig. 2[28]), reversible cerebral vasoconstriction syndrome, pituitary apoplexy or arterial dissection.

Box **Selected possible causes of thunderclap headache in order of frequency**[22-24]

- Subarachnoid haemorrhage
- Reversible cerebral vasoconstriction syndrome
- Cerebral venous thrombosis
- Other primary headache: primary thunderclap, cough, sexual and exertional headaches
- Cervical artery dissection
- Infection (e.g. sinusitis, meningitis, encephalitis)
- Spontaneous intracranial hypotension
- Stroke (haemorrhagic or ischaemic)
- Posterior reversible encephalopathy syndrome
- Pituitary apoplexy
- Third ventricular colloid cyst
- Sentinel headache (preceding a subarachnoid haemorrhage)
- Retroclival haematoma

Fig. 1 **Diffuse subarachnoid haemorrhage on a CT scan**[25]



Full evaluation for a patient with a thunderclap headache therefore includes non-contrast CT, with a lumbar puncture if the onset was more than six hours before, or the image is technically inadequate.[27] When subarachnoid haemorrhage is excluded, there are many alternative diagnoses to consider (see Box).[22] MRI with venography and angiography is recommended for investigating these causes.[23]

Disorders of intracranial pressure

Patients with a history or clinical examination suggestive of raised intracranial pressure always require further investigation. This is to exclude hydrocephalus, a space-occupying lesion and cerebral venous sinus thrombosis. Ideally, MRI of the brain and orbits and venography are performed.[13] MRI features in keeping with raised intracranial pressure include flattening of the globe, optic nerve distension or tortuosity, empty sella, posterior displacement of the pituitary stalk, slit-like ventricles and an inferior position of the cerebellar tonsils (see Fig. 3[29]).[30] However, MRI findings are not pathognomonic, nor does their absence completely exclude idiopathic intracranial hypertension, so all patients with papilloedema should be referred for expert opinion. Conversely in patients with spontaneous intracranial hypotension, MRI may reveal diffuse pachymeningeal enhancement, descent of the tonsils (mimicking the Chiari I malformation), hygromas, or engorgement of the pituitary and the cerebral venous sinuses.[31] These patients generally require expert evaluation and management.

Fig. 2 **CT venogram showing extensive venous thrombosis in the superior sagittal sinus**[28]

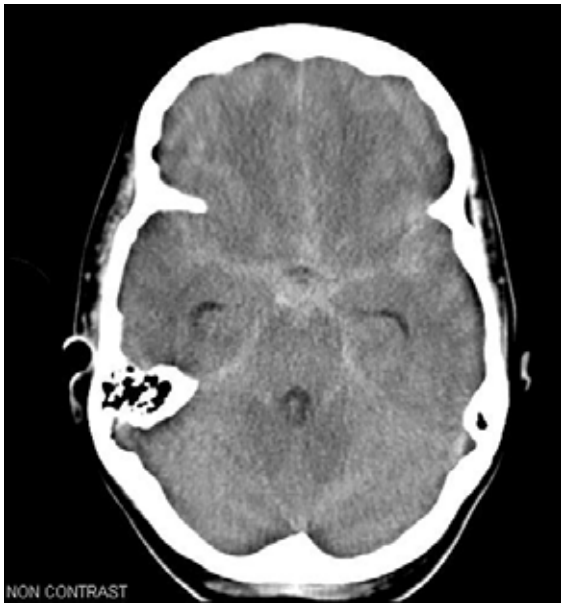
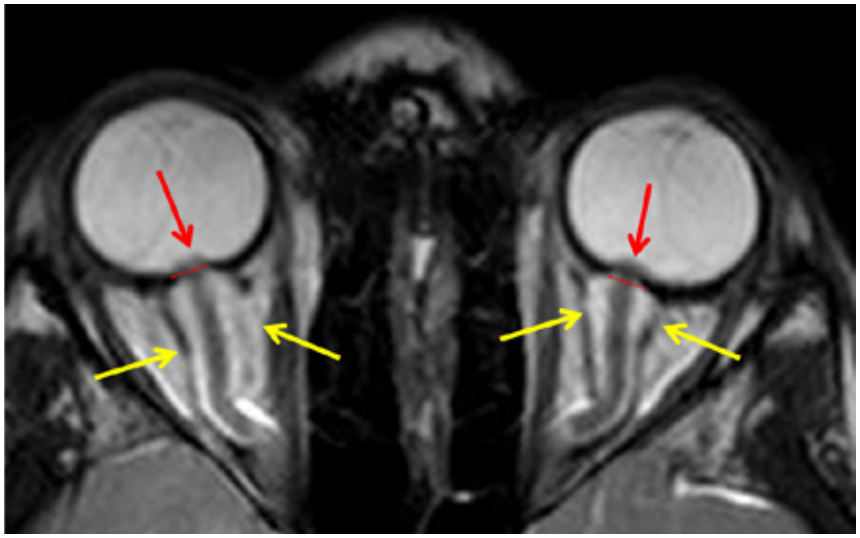


Fig. 3 **A case of idiopathic intracranial hypertension**[29]



MRI shows flattening of the posterior sclera, intraocular protrusion of the optic nerve head (red arrows) and tortuous optic nerves with prominent subarachnoid space (yellow arrows).

Conclusion

The overall rate of significant pathology found on MRI is relatively low, with incidental findings in approximately 2% of people. Investigation should therefore be guided by a thorough clinical assessment, to ensure the appropriate type and speed of investigation. ≺

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Elspeth Hutton has served on advisory boards for Sanofi-Genzyme, Novartis, Teva, Eli Lilly, Allergan, Lundbeck, been involved in clinical trials sponsored by Novartis, Teva, Xalud, Daewong and Novotech, and received payment for educational presentations from Allergan, Teva, Eli Lilly and Novartis.

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