HEADACHE – Common symptom with Rare Diagnosis in UK Primary Care – A Case report

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Abstract

Headache is a common presenting symptom in Primary Care with a wide list of differential diagnoses and important red flag symptoms.

It is vital in Primary Care to undertake a comprehensive history, careful examination and appropriate investigations when patients present with any of these symptoms. Clinicians should be mindful of the differential diagnoses and red flag symptoms in order to appropriately manage patients. It is also crucial to recognise when to get help from secondary care colleagues when faced with rare and complex cases that may need hospital admission for further investigations, management and monitoring.

This case highlighted the importance of being aware of different, including rare, differentials when confronted with a common presenting symptom.

Keywords: headache, rare diagnosis, Reversible Cerebral Vasoconstriction Syndrome (RCVS).

Headache prevalence

• Headache is a common symptom in Primary care.

o A cross-sectional study using structured questionnaires (n = 8,271 from 10 European countries including Austria, France, Germany, Ireland, Italy, Lithuania, Luxembourg, Netherlands, Spain and United Kingdom) found the lifetime prevalence of headache to be 91.3% and the annual prevalence 78.6% [Steiner, 2014].

• Most patients self-manage their headaches, yet it still remains one of the commonest reasons for consulting in Primary Care.

o An analysis of records from 253 UK General Practices found that approximately 4% of adults consult their GP for headache each year (6.4% per year in women and 2.5% per year in men) [Latinovic, 2006].

o Approximately 2% of people seen in General Practice with headache are referred to a neurologist [Latinovic, 2006].

• The majority of headaches are primary (approximately 90%).

o The three most common types of primary headache are tension-type headache (40%), migraine (10%) and cluster headache (1%) [Hainer, 2013; Hale, 2014].

Headache – with rare diagnosis – A Case report from UK Primary Care

A 41 year old lady presented with a one day history of sudden onset severe headache, described as the "worst ever", which intensified over a few minutes. This is a description in keeping with a "Thunderclap Headache"; a well known red flag symptom.

It was associated with photophobia and nausea.

She denied any neck stiffness, loss of consciousness, fits, weakness of upper or lower limbs, slurring of speech, visual disturbance or dizziness.

She had no significant past medical history or previous history of headache and she was not taking any regular medication.

She was an ex-smoker. She did not drink alcohol.

On examination, the cardiorespiratory systems and Peripheral neurological examinations were normal. Cranial nerves were intact. Fundoscopy was normal and, in particular, no papilloedema was noted. ENT examination was also normal.

Observations were unremarkable: BP 143/79; Pulse 88 and regular; Temp 36.7 degrees Celsius; Oxygen Saturation 98 % on air.

She was referred to the hospital and admitted by the on call medical team. She was examined, underwent blood tests and received a CT head scan; all of which were reported as normal. She was thus discharged home with a provisional diagnosis of Migraine or Tension type headache with appropriate safety netting advice.

She presented to the Emergency Department three days later with the same severe headache but now occurring in episodes described as "worst ever" and lasting for a few minutes to a couple of hours each time. Furthermore, she now had associated vomiting with the episodes and generally felt unwell. She was readmitted to the medical ward. A repeat CT head scan showed bilateral Parietal Parenchymal Haemorrhage and a Subarachnoid Haemorrhage.

To further evaluate these findings she had a CT angiogram (CTA) which showed multi focal narrowing on the Pericallosal arteries as well as the middle cerebral and vertebral arteries, features suggestive of Reversible Cerebral Vasoconstriction Syndrome (RCVS).

A follow up MR Angiogram confirmed multi-vessel narrowing without focal wall enhancement, again suggestive of RCVS. The subarachnoid and left hemisphere Parenchymal haemorrhages showed the expected evolution.

MR Cervical Spine and Echocardiogram were both reported as normal.

She was treated with Nimodipine 60mg three times daily and discharged. On review by the neurologist at 4 weeks post discharge she reported feeling much better. The patient remains under the care of the neurologist with a plan to discontinue the medication if she remains symptom free, and, if follow up imaging, planned at 12 weeks post discharge, is normal.

Discussion

This case was both interesting as well as challenging due to the initial normal examination and investigations, including a normal CT scan of the head. This is often the case in RCVS. It served as a reminder that even common presentations such as headache may on occasion be symptomatic of rarer or more complex pathology as is the case in RCVS. Hence clinicians should adopt an open minded approach, particularly if the patient's symptoms are not resolving, and be prepared to reconsider the initial diagnosis.

In summary, the key learning points from this case were:

• Specifically, be aware of RCVS as a potential differential diagnosis in patients with headache.

• More generally, to re-evaluate and reconsider the diagnosis if the patient continues to have symptoms despite normal initial investigations.

• To recognise red flag symptoms in primary care and act accordingly and in a timely fashion. For example, a first presentation of thunder clap headache should prompt immediate referral to hospital for same day specialist assessment.

What is Reversible Cerebral Vasoconstriction Syndrome (RCVS)

Reversible cerebral vasoconstriction syndrome (RCVS) is a relatively recently described condition characterised by sudden, severe ('thunderclap') headache; with or without other acute neurological symptoms and diffuse segmental constriction of cerebral arteries that resolves spontaneously within 3 months.

Reversible cerebral vasoconstriction syndromes are clinically important because they affect young persons and can be complicated by ischaemic or haemorrhagic strokes. The differential diagnosis of RCVS includes conditions associated with thunderclap headache and conditions that cause irreversible or progressive cerebral artery narrowing, such as intracranial atherosclerosis and cerebral vasculitis. Misdiagnosis as primary cerebral vasculitis and aneurysmal subarachnoid haemorrhage is common because of overlapping clinical and angiographic features. However, unlike these more ominous conditions, RCVS is usually self-limiting: resolution of headaches and vasoconstriction occurs over a period of days to weeks.
More than half the cases are seen in the post-partum period or after exposure to adrenergic or serotonergic agents. It affects all ages, mean age of onset is 42 years, and women are affected more than men.

RCVS is thought to be responsible for the majority of benign thunderclap headaches.

History and etymology

Case studies of the condition first appeared in the 1960s, but it was not then recognised as a distinct entity. In 1983, French researchers published a case series of 11 patients, terming the condition acute benign cerebral angiopathy. Gregory Call and Marie Fleming were the first two authors of a report in which doctors from Massachusetts General Hospital, led by C. Miller Fisher, described 4 patients, alongside 12 previous case studies, with the characteristic symptoms and abnormal cerebral angiogram findings. The name Call-Fleming syndrome refers to these researchers.

A 2007 review by Leonard Calabrese and colleagues proposed the name reversible cerebral vasoconstriction syndrome, which has since gained widespread acceptance. This name merges various conditions that were previously treated as distinct entities, including Call-Fleming syndrome, postpartum angiopathy, and drug-induced angiopathy. Other names may still be used for particular forms of the condition.

Clinical Features of RCVS

The condition is usually acute and self-limiting without the appearance of new symptoms after one month. RCVS may present as a thunderclap headache (TCH) in isolation or as TCH with associated neurologic symptoms.

Headaches remain the main and often the only manifestation in these patients.

- Presents with acute headaches - thunderclap headaches.
- Pain may last for a few minutes to a few hours.
- Typically bilateral (but can be unilateral), with posterior onset followed by diffuse pain.
- Screaming, crying, agitation, confusion and collapse are common due to the severity of the pain.
- Nausea, vomiting, photophobia, and phonophobia is frequently seen.
- Multiple episodes of thunderclap headaches are seen which recur approximately every day for a few days up to four weeks (but a single attack is also possible).
- Between exacerbations the patient may complain of a persistent moderate headache.
- In about a third of patients, a surge in blood pressure can be observed during acute headaches.

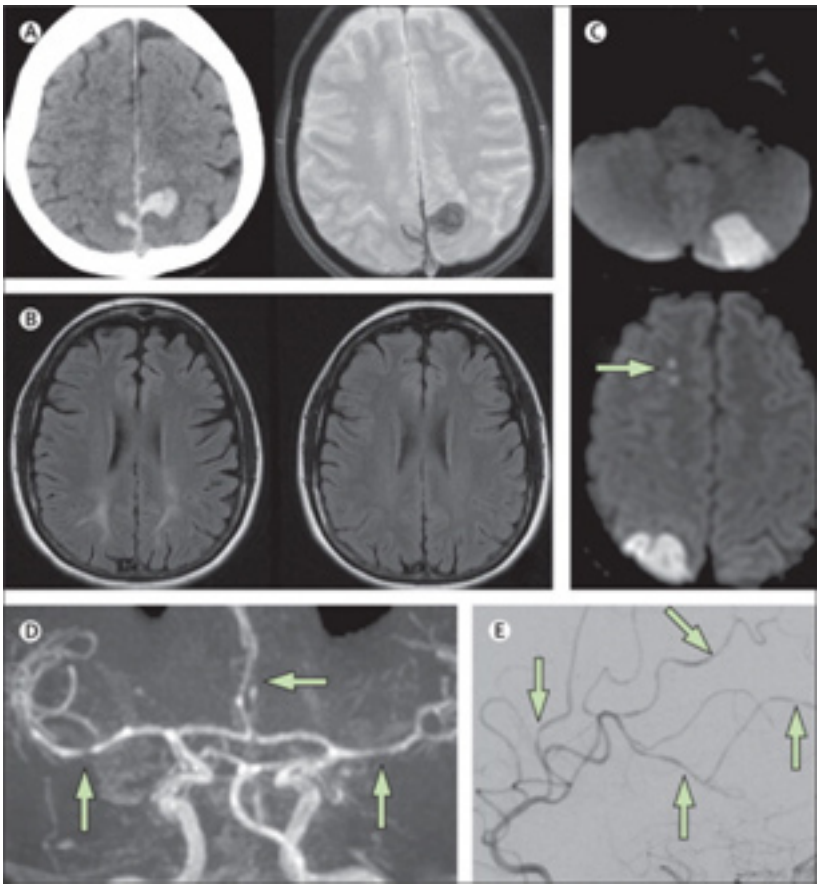
Precipitants of Reversible Cerebral Vasoconstriction Syndrome

- Post-partum period
- Vasoactive drugs
    - o illicit drugs e.g., cannabis, cocaine
    - o Antidepressants e.g., selective serotonin reuptake inhibitors, serotonin-noradrenaline reuptake inhibitors
    - o Sympathomimetics e.g., nasal decongestants (phenylpropanolamine, pseudoephedrine, ephedrine), norepinephrine
    - o Binge drinking
- Catecholamine-secreting tumours e.g., Phaeochromocytoma, bronchial carcinoid tumour
- Immunosuppressants or blood products e.g. - intravenous immunoglobulin, red-blood-cell transfusion, interferon alfa
- Miscellaneous e.g. - hypercalcaemia, porphyria, head trauma, neurosurgery, subdural spinal haematoma, carotid endarterectomy, cerebral venous thrombosis, CSF hypotension

Neuroimaging for RCVS

RCVS with isolated headache will show a normal plain CT brain. However, as the condition progresses the presence of segmental narrowing and dilatation ('string of beads') of one or more cerebral arteries, seen on magnetic resonance angiography (MRA) or CT angiography (CTA), becomes diagnostic of RCVS.

Figure: Lesions in patients with reversible cerebral vasoconstriction syndrome



Proposed diagnostic criteria for reversible cerebral vasoconstriction syndrome:

• Acute and severe headache (often thunderclap) with or without focal deficits or seizures.
• Uniphasic course without new symptoms more than one month after clinical onset.
• Segmental vasoconstriction of cerebral arteries shown by indirect (e.g., magnetic resonance or CT) or direct catheter angiography.
• No evidence of aneurysmal subarachnoid haemorrhage.
• Normal or near-normal CSF (protein concentrations <100 mg/dL, <15 white blood cells per µL).
• Complete or substantial normalisation of arteries shown by follow-up indirect or direct angiography within 12 weeks of clinical onset.

Other causes of thunderclap headaches should be considered in the differential diagnosis.

Note:

• Clinicians should note that early investigations (MRA, CTA, and even catheter angiography) may be normal up to six or seven days after headache onset in patients who are ultimately shown to have RCVS on repeat angiography.
• Haemorrhagic and ischaemic stroke can occur, sometimes after a few days of isolated headaches in patients with initial normal brain imaging.

Management of RCVS

There is no evidence-based treatment for RCVS. Early recognition of the syndrome is important to manage symptoms.

Spontaneous resolution usually occurs, with improvement in angiographic findings within three months. The natural history of the condition has not however been well characterised. Complete long-term resolution of the symptoms with no neurological deficit is the most common outcome in up to 90% of patients.

• Remove any precipitating or aggravating factors
    o Patients should be advised to rest (some patients need bed rest in hospital for two weeks) and to avoid sexual activity, physical exertion, Valsalva manoeuvres, and other triggers for a few days to a few weeks (depending on the initial severity).
    o Vasoactive drugs should be discontinued (avoided even after disease resolves).

• Drug treatment to relieve vasospasm:
o Nimodipine, Verapamil and Magnesium sulphate have been used. Although no randomised controlled trials are available, treatment with calcium channel blockers seems to be efficacious and are thought to be a reasonable first-line therapy. Short course glucocorticoid therapy has also been advocated.

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