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Case Report | Peer-Reviewed Article

Headache and Transient Neurological Symptoms

22-year Post-Partum Woman

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Abstract

Introduction: Postpartum headache is a frequently encountered clinical scenario. We describe a case of a 22-year-old woman presenting with severe postpartum headache associated with transient neurological symptoms.
Methods: We encountered the case in routine clinical practice.
Results: A 22-year-old woman, with no significant previous history of headache, developed holo-cranial post-partum pain, associated with transient episodes of hemi-sensory loss, hemiparesis and slurring of speech. Imaging revealed T2/FLAIR hyper-intensities in frontal-parietal and temporal regions and in the bilateral subcortical region with patchy focal diffusion restriction. Her basic labs, metabolic and immune workup were normal, along with an acellular normal-proteomic cerebrospinal fluid analysis. Visual evoked potentials showed bilateral prolonged latencies. Considering her family history of early stroke and temporal lobe hyper-intensities, genetic analysis for NOTCH3 gene was done, which came back positive.
Conclusion: This case describes a postpartum onset of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) with non-migrainous headache. Furthermore, it highlights that a comprehensive history backed by targeted investigations is the right approach to evaluate neurological conditions.
Keywords: CADASIL; post-partum headache

Case Report

A 22-year-old woman with no previously diagnosed neurological conditions, and an uneventful antenatal period presented at 37 weeks of gestation to her obstetrician with intermittent episodes of headaches. The headaches were described as bitemporal, throbbing, lasting five to ten minutes, present for about five days, 3/10 on the visual analogue pain scale, not associated with photophobia, phonophobia, nausea or vomiting with no history of diplopia, blurring of vision, loss of consciousness or seizure. Examination revealed a normal fundus and an elevated blood pressure (BP) of 150/90 mm Hg, which subsequently normalized on antihypertensives. Further neurological examination was unremarkable. Her BMI prior to pregnancy was 22.9 kg/m^2 and presently 27.3 kg/m^2. The patient was taken up for an elective lower segment caesarean section the following day and a healthy female baby was delivered. Three hours later, she experienced severe pain in the high parietal region that spread holo-cranially over 30 minutes, dull aching, not aggravated by bending or coughing and not relieved with analgesics. The pain was associated with photophobia, five to six episodes of non-projectile vomiting, but no phonophobia, diplopia, blurring, neck pain, postural aggravation or loss of consciousness was experienced. Subsequently, she reported five to six episodes of left upper limb and left facial numbness with an occasional slurred speech lasting around ten minutes with complete recovery. One of the episodes was additionally characterized by right upper limb weakness noted when she had difficulty drying herself with a towel. She was aware of the episodes, with no evidence of tonic or clonic movement, incontinence, or up-rolling of eyes. Her headache was near-continuous and progressed to severity. Fundoscopy was normal.

At this point, the following differentials were entertained: posterior reversible encephalopathy syndrome (PRES), cerebral venous thrombosis, postdural puncture headache, reversible cerebral vasoconstriction syndrome, pre-eclampsia and central nervous system vasculitis.

The initial non-contrast magnetic resonance imaging (MRI) of the brain, done when the headache had started, showed bilateral symmetrical T2/FLAIR hyperintensities along the bilateral periventricular and deep white matter of frontal, parietal and temporal lobes with no evidence of diffusion restriction (fig. 1A-D). Axial T2 images demonstrated a high T2 signal expanding the dural sheath of optic nerves bilaterally. Magnetic resonance angiogram and venogram were normal.

On further probing, she gave no prior history of significant recurring or chronic headaches and explained that her symptoms had dramatically worsened in the three days before she presented to our hospital. On examination, the patient had normal BP while on two antihypertensives and had no focal deficit. Her blood routines, including hemogram, renal and liver profiles, glycemic and thyroid status, showed normocytic normochromic anemia with low iron and ferritin values and marginally elevated lactate dehydrogenase and fibrinogen with a normal thyroid profile. Her erythrocyte sedimentation rate, C-reactive protein, ANA, ACE levels, P-ANCA, C-ANCA, and ENA levels were within normal limits.

Gadolinium-enhanced MRI of the brain was conducted, which showed similarly distributed bilateral symmetrical T2 /T2 FLAIR hyperintensities with scattered areas of patchy focal diffusion restriction seen in right corona radiata, right lentiform nucleus left frontal and parietal lobes (fig. 1E) with no abnormal contrast enhancement and lesions being perpendicular to the lateral ventricle.

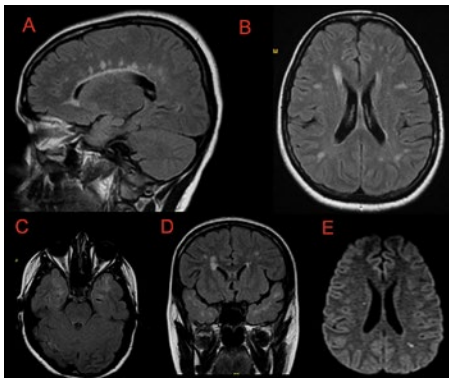

Figure 1: Magnetic resonance imaging (MRI) FLAIR sequence sagittal (A), axial (B, C) and coronal (D) cuts demonstrating periventricular and deep white matter hyperintensities of frontal, parietal and temporal lobes. MRI axial diffusion-weighted image (E) shows restricted diffusion in the right corona radiata and left parietal lobe.

Lumbar puncture was performed, which found a cerebrospinal fluid opening pressure of 20 cm H20, cells 4, glucose 58 (corresponding blood glucose 89 mg/dl) and protein 65.9. Gram stain, culture, geneXpert for *mycobacterium tuberculosis*, potassium hydroxide preparation for fungus, adenosine deaminase and oligoclonal bands (OCB) were sent and came back negative.

At that point, on further probing, she revealed that her mother had a stroke at forty-five years but further reports were unavailable. In view of persisting headache with photophobia, transient neurological symptoms, a history of young stroke and with T2 hyperintensities in the anterior temporal lobe, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) was considered as a possibility. However, sudden onset headaches in the postpartum period with no prior history suggestive of migraine and visual evoked potential (VEP) prolongation were points against CADASIL. NOTCH3 analysis showed a heterozygous missense variant in exon 4 of the NOTCH3 gene that resulted in the amino acid substitution of cysteine for arginine at codon 133 and was classified pathogenic. Low-dose aspirin was initiated along with risk factor management and analgesics.

Discussion

CADASIL is an autosomal dominant inherited angiopathy caused by mutation of the NOTCH3 gene on chromosome 19 reported to be the most common heritable cause of stroke and vascular cognitive impairment in adults [1]. Though studies claim prevalence of cysteine altering NOTCH 3 variants to be as high as 1 in 300 in the Western world, the exact prevalence in India is still unknown [2]. It has a wide spectrum of clinical presentation, including migraine with aura, stroke in young, transient ischemic attack (TIA), acute reversible encephalopathy, cognitive impairment, dementia, neuropsychiatric symptoms, and seizures. In a study by Roine et al. regarding CADASIL and pregnancy, 48% of CADASIL patients developed neurological symptoms during pregnancy, of which 82% experienced neurological manifestations for the first time [3].

In this case, atypical PRES was considered, given her elevated BP on admission, but the distribution of the lesions with diffusion restriction made it less likely. Moreover, during the entire course, her BP remained normal. Spontaneous intracranial hypotension (SIH) was kept in the differentials due to the occasional orthostatic component described by the patient. But the absence of patchy-meningeal enhancement and other radiological features of SIH, such as the flattening of the pons, venous engorgement, pituitary hyperplasia and the presence of the above radiological features made it less likely. The high T2 signal expanding the dural sheath of optic nerves bilaterally plus bilaterally prolonged latencies VEP, could also elicit a diagnosis of idiopathic intracranial hypertension, but the normal opening pressure on lumbar puncture makes it less likely; this T2 signal expanding the dural sheath of optic nerves therefore remains unexplained. Preeclampsia was a possibility, but the patient had no additional end-organ dysfunction (normal liver and renal function tests, urine proteins, platelet count and absence of visual symptoms). Lastly, Susac syndrome was considered, given that this was a young woman with lesions in the corpus callosum, but the absence of hearing loss, visual symptoms and encephalopathy was contradictory.

Since the MRI showed T2/FLAIR lesions perpendicular to the lateral ventricle, lesions in the cortical regions, and patchy focal diffusion restriction distributed across periventricular and cortical territories, the possibility of multiple sclerosis (MS) was considered in the differentials. VEP of both eyes showed a bilateral prolonged P100 response suggestive of an anterior visual pathway defect. However, the patient's clinical symptoms were mainly headache, with the other sensory-motor symptoms lasting only for ten minutes during each episode, with no focal deficit on examination. This made the possibility of MS less likely.

Differentiating MS from CADASIL still poses a dilemma, especially with recent case reports claiming both can occur concomitantly [4]. Clinical presence of migraine, TIA-like episodes, a positive family history, seizures, and cognitive decline all favor CADASIL, whereas the presence of MS-defining clinical syndromes, optic neuritis and spinal cord involvement, may tilt the balance in favor of MS. Our patient had a headache which was not migrainous and not a MS-defining symptom as well as TIA-like episodes, none of which lasted over an hour. Radiologically, involvement of the anterior temporal lobe and external capsule is almost diagnostic of CADASIL, although other features like subcortical involvement, presence of cerebral microbleeds and cerebral atrophy may also aid in the diagnosis. The pattern of involvement and lesion characteristics can mimic MS [5]. We cannot rule out that the patient's unusual symptoms were related to a disease in addition to her CADASIL, such as eclampsia, PRES, atypical MS, or idiopathic hypertension, as recently described in another peripartum patient [6].

The absence of oligoclonal bands on lumbar puncture also favors CADASIL, but OCBs have also been found [7]. Moreover, VEP abnormalities have been noted in CADASIL patients with a mean P100 delay of 114 ms by Parisi et al. [8]. This case highlights the need for goal-directed testing, as many of the investigations are expensive. An incorrect diagnosis of MS would have resulted in unnecessary psychological, financial and therapy-related burden for both the patient and their family. This case describes a postpartum onset CADASIL with severe non-migrainous headache and transient focal symptoms. Furthermore, it highlights, that a comprehensive history-taking and clinical evaluation backed by directed investigations is the right approach in evaluating neurological conditions.

Highlights

- CADASIL can be unmasked for the first time during pregnancy or in the peripartum period, even with no prior history suggestive of migraine.
- Imaging features of CADASIL can closely resemble multiple sclerosis, with even VEP and OCB being positive. But careful examination of the history and specific imaging characteristics can be revealing.
- Comprehensive history-taking with directed investigations is the right approach to evaluate any neurological symptom.

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Ethics Statement

Informed consent was obtained.

Conflict of Interest Statement

No financial support and no other potential conflict of interest was reported.

Author Contributions

Dr Uma Ravishankar: Drafting and data acquisition.
Dr Rithvik Ramesh: Conception and design, data acquisition, interpretation, drafting and revision.
Dr Shankar V: Final approval.
Dr Sundar S: Conception, Data acquisition, final approval.
Dr Philo Hazeena: Drafting and revising for critical intellectual content.

Data Availability Statement

The datasets used and/or analyzed are available from the corresponding author on reasonable request.

References

You will find the full list of references online at https://cvm.swisshealthweb.ch/en/article/doi/cvm.2023.1173847998/.

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