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Status Migrainosus: Refractory Headache in a Woman with Pre-eclampsia

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ABSTRACT

Headaches in pregnancy are common and carry a range of differential diagnoses. When faced with this diagnostic conundrum, it is important to consider and exclude sinister aetiologies such as pre-eclampsia and hemorrhagic stroke. A differential diagnosis of migraine is also warranted, given the high burden of migraine in young women. We report a case of refractory headache in a primiparous woman, resulting in an admission to the Intensive Care Unit (ICU), requiring multiple antihypertensive medications despite a negative preeclampsia screen. The woman was ultimately diagnosed with status migrainosus, resolving with the administration of a Chlorpromazine infusion. We highlight the difficulties involved in identifying and treating severe headaches in pregnant women.

Keywords: Migraine; Pre-eclampsia; Headache; Antenatal; Postnatal; Status migrainosus

INTRODUCTION

Status migrainosus is diagnosed when a migraine episode persists for more than 72 hours and is refractory to usual treatment [1]. The presentation of headache in pregnancy presents a diagnostic dilemma as several sinister pathologies have similar symptom profiles (Central Venous Sinus Thrombosis (CVST), tumour and haemorrhagic strokes) [2]. Migraines occur commonly in pregnancy and are difficult to differentiate from these more sinister aetiologies. They are also difficult to treat due to the teratogenic properties of several prophylactic medications if given antenatally, and vertical transference during breastfeeding [3]. There is little documentation of status migrainosus in pregnancy, which provides further challenges for diagnosis and treatment in this small patient population.

CASE PRESENTATION

A 31-year-old primiparous woman (G4P0) was seen on multiple occasions throughout her pregnancy for headaches. She had a high risk for PET based on her low PAPP-A of 0. 36 MoM, thus was placed on low-dose aspirin at 13 weeks gestation. She had a past medical history of anxiety and depression, with no history of previous migraines or neurological issues.

Initially she presented to the birthing unit with a headache and hypertension at 31+2 weeks gestation. She described intermittent headaches occurring from 20 weeks' gestation, worsening in intensity, duration and frequency. Blood pressure was initially 150/90 mmHg, well controlled with an initial dose of 100mg Labetalol. Urine protein-creatinine ratio (uPCR), and pre-eclampsia biochemistry (inclusive of platelets, liver

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function, coagulation and renal function tests) were negative. Paracetamol was minimally effective for the management of her headache. She was diagnosed at this stage with gestational hypertension (gHTN) and was commenced on Labetalol 100 mg TDS. Fetal growth and wellbeing ultrasound showed normal growth and dopplers.

She represented at 34+6 weeks gestation with ongoing headaches, stating they were unchanged since her previous presentation. Examination was normal, BP 140/82 mmHg, with a negative uPCR and PET serology screen. She was commenced on 25 mg Sumatriptan PRN which improved her headache.

At 37+0 the patient represented with worsening headaches and diplopia. Peripheral oedema was evident on examination. BP was initially 148/98 mmHg but became increasingly difficult to manage, requiring additional antihypertensives. She was admitted to maternity, commenced on hydralazine 50 mg TDS and her labetalol increased to 200 mg TDS. PET serology and uPCR remained negative, fetal monitoring and ultrasounds remained stable.

She underwent an induction at 37+2 weeks gestation, during labour she requested an epidural insertion (uncomplicated) and was delivered with forceps for fetal bradycardia. She had an otherwise uncomplicated labour.

On review day one postpartum, the patient described severe retroorbital headaches, which were not positional. She was reviewed by the anaesthetic team who deemed the symptoms unlikely secondary to a Post Dural Puncture Headache (PDPH).

Day two postnatally, the patient developed severe hypertension (BP 190/120 mmhg) with no neurological examination findings. Management initially involved a regular regime for severe preeclampsia: requiring four hypertensive agents, intravenous hydralazine and magnesium sulphate infusions. Due to the unstable hypertension and commencement of a hydralazine infusion, the patient was admitted to ICU. PET serology and uPCR remained negative.

During her ICU admission, the patient's headache was still severe and uncontrolled, neurological signs developed, with left sided clonus and hyperreflexia. She was commenced on a fentanyl infusion for the management of her headache. The neurology team was consulted who recommended investigations including a non-contrast CT brain, MRI, MRA and MRV, which excluded structural pathology. Neurology consultation ultimately resulted in a diagnosis of status migrainosus.

Subsequently, the woman was commenced on an infusion of 12.5 mg Chlorpromazine (5 doses in total), an oral course of 25 mg Prednisone and Amitriptyline 10 mg, which resolved her hypertension and headache. She remained in ICU for two days and was discharged from the maternity unit on day six postpartum. Treatment with Onabotulinum Toxin-A was commenced three weeks later. The woman remained symptom-free at her postpartum follow up.

DISCUSSION

Headaches in pregnancy present a diagnostic conundrum, as typical migraine-associated features are difficult to distinguish from preeclampsia [4]. Both conditions similarly present with severe headache and visual disturbances. In addition, other high risk causes of headache such as stroke, tumour, idiopathic intracranial hypertension, CVST and pituitary apoplexy also warrant prompt exclusion in pregnancy [4].

Symptoms suggestive of status migrainosus include headaches, with or without aura, vomiting, irritability and diarrhea. Migraines have a well-documented pathophysiological link with sex hormones, with abrupt decline in estrogen levels triggering the onset of migraine [5]. The onset of post-partum migraine may be explained by a steep decline in oestrogen levels following delivery.

Severe postpartum headache requires diligent investigation. In this case, the woman's headaches were unresponsive to standard treatments for pre-eclampsia and hypertension. Only after the administration of a Chlorpromazine infusion the headaches resolved [6], confirming a diagnosis of refractory migraine. As the woman had already been appropriately treated for pre-eclampsia, the Neurology team could proceed exploring other differential diagnoses and ultimately managing the migraine. Management, guided by the neurology team, including further magnesium sulphate and steroids. Oral corticosteroids (prednisone or dexamethasone) have been documented to improve headache recovery and reduce relapse [7]. Magnesium sulphate infusions have also been documented to decrease neurological excitation in previous case studies [8].

Chlorpromazine is a dopaminergic antagonist, which has anxiolytic, antiemetic and sedative properties. However, the precise pathophysiology behind its efficacy in migraine remains unknown.

Treatment options are limited antenatally due to the potential teratogenic effects on the fetus. Acutely, if recurrent migraines occur in pregnancy; paracetamol, sumatriptan, metoclopramide and ondansetron are considered safe. Migraine prophylaxis may be considered with long term propranolol, or lamotrigine as they have excellent safety profiles in pregnancy [9].

Other antenatal prophylactic options include peripheral nerve blocks, non-invasive stimulation devices or botulinum toxin injections [10]. These therapeutic options may be explored antenatally to prevent difficult clinical situations such as the case described here.

Peripheral nerve blocks involve injecting 2% lidocaine, along with dexamethasone or methylprednisolone, adjacent to a peripheral nerve (most commonly the great occipital nerve) [11]. Non-invasive topical devices (such as the Cefaly or transcranial magnetic stimulation device) are also low risk treatment options. Botulinum injections have limited data in pregnancy, however, may be considered if other forms of therapy have failed [12].

Nonpharmacologic therapies such as cognitive behavioural therapy, acupuncture and relaxation exercises have shown some benefit [13,14]. Antenatally, women with migraines should be educated around potential triggers, such as hunger, sleep deprivation and dehydration.

During the postpartum period, options for treatment are widened, however considerations for transference to breastmilk must be considered. Compatible pharmacological therapy during breastfeeding includes ibuprofen, triptans, beta blockers, valproate, lamotrigine and amitriptyline [15].

CONCLUSION

There is little documentation of the management of status migrainosus in pregnancy, making management difficult. While management options for migraine prophylaxis during pregnancy and breastfeeding are limited, effective treatments are available. Early Neurology consultation is advisable to prevent the occurrence of severe migraine symptoms during pregnancy. However, when severe symptoms do occur, as in this case, a thorough set of investigations to exclude sinister aetiologies must be undertaken. We also propose that it is reasonable to commence empirical treatment for pre-eclampsia, particularly in the presence of concomitant hypertension, as there are no clinical features that allow for a clear distinction between pre-eclampsia and migraine.

CONFLICT OF INTERESTS

The Author(s) declare(s) that there is no conflict of interest.

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INFORMED CONSENT

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

ETHICAL APPROVAL

Ethics approval to report this case was obtained from the Northern Beaches Hospital Research Governance Committee

CONTRIBUTORSHIP

Dr Swain wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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