J Anesth (2013) 27:757–760
DOI 10.1007/s00540-013-1586-8

CLINICAL REPORT

Third nerve palsy associated with preeclampsia and HELLP syndrome

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Received: 7 November 2012 / Accepted: 21 February 2013 / Published online: 12 March 2013

Abstract Preeclampsia can cause myriad organ dysfunction, including cranial nerve palsies that pose diagnostic and management dilemmas. We present an unusual case of third nerve palsy, (presenting as diplopia, ptosis) with hypertension, hyperreflexia, proteinuria, easy bruising in a parturient at 34 + 6/52 weeks of twins gestation. She was treated as for severe preeclampsia and HELLP syndrome; intravenous magnesium sulphate and labetalol commenced and emergent cesarean delivery performed under general anesthesia due to concerns of low platelets and for airway protection should her glascow coma scale (GCS) deteriorate. Postoperatively, stroke, aneurysm and intra-cerebral causes of third nerve palsy were excluded, with subsequent recovery of symptoms upon blood pressure normalization. The eye signs are postulated to be due to two preeclamptic mechanisms involving disordered cerebral autoregulation: (1) hyperperfusion and breakdown of the blood–brain barrier that occurs with rising hypertension, causing fluid/blood product extravasation into brain parenchyma, or (2) focal reactive vasoconstriction and local hypoperfusion, contributed to by endothelial dysfunction.

An abstract of this study was presented in part at the 13th Asian Australasian Congress of Anaesthesiologists in Fukuoka, Japan. June 1–5, 2010.

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Keywords Preeclampsia · HELLP · Third nerve palsy

Introduction

Preeclampsia affects a myriad of systems in a pregnant woman, and its etiology remains unclear. Causes range from maternal immune reaction to the inadequately implanted placenta [1], to oxidative stress damaging the endothelium [2]. It commonly presents with hypertension, proteinuria [3], and neurological complications including seizures, strokes, and rarely, cranial nerves palsies.

Case report

A 31-year-old woman, gravida 2 para 0, weight 73 kg, height 1.74 m, BMI 24 kg/m^2, was pregnant with twins after in vitro-fertilization. During a routine antenatal visit at 34 weeks of gestation, she recorded a blood pressure (BP) of 147/79 mmHg and proteinuria. As she was otherwise well, the obstetrician managed her expectantly without anti-hypertensives.

Six days later, she was admitted emergently with diplopia, drooping of the right eyelid. She was found to have generalized hyperreflexia without clonus, bibasal lung crepitations, BP 151/95 mmHg, pulse 110 beats per minute. She was alert, lucid, denied any headache or right upper quadrant/epigastric pain. A loading dose of 4 g of IV magnesium sulphate was given followed by an infusion of 1 g/h. In view of impending eclampsia, viable fetuses, and inability to organise expedient neuroimaging, the obstetric team chose to proceed with emergency cesarean section. This was performed under general anesthesia (GA) on clinical suspicion of disordered coagulation and low

platelets (she exhibited easy bruising and longer bleeding times upon intravenous cannulation).

Two viable infants were delivered, a 2,090 g male, and a 2,215 g female, with APGAR scores 5 and 8 at 1 min, and 9, 9 at 5 min respectively. She was hemodynamically stable throughout the 34 min cesarean delivery. Blood loss was 800 ml, urine output was 150 ml. The results of the blood investigations taken prior to the operation became available at the completion of surgery, showing a platelet count of 54×10^9/l, hemoglobin level of 13.8 g/dl, white cell count of 6.83×10^9, creatinine of 90 μmol/l, and normal coagulation. There was elevated uric acid (552 μmol/l) and liver enzymes (alkaline phosphatase 197 U/l, aspartate transaminase 40 U/l). She was sent to our obstetric intensive care unit (ICU) post operatively for monitoring of her severe preeclampsia and possible HELLP (hemolysis, elevated liver enzymes, and low platelet) syndrome.

An arterial line was inserted, and IV magnesium sulphate infusion continued. Blood pressure was controlled with oral labetalol 100 mg tds on the first post-operative day, and increased to 150 mg tds the next day, achieving a target blood pressure of less than 140/90 mmHg. She was given patient-controlled analgesia with IV morphine.

Detailed examination in the ICU post-cesarean revealed a right partial ptosis, binocular diplopia, and limited adduction, elevation and depression of the right eye. The right pupil was dilated 6 mm with decreased reactivity to light. Generalized hyperreflexia was present (no clonus), and there were no other neurological deficits or papilledema. Subsequently, cranial magnetic resonance imaging excluded an intracranial hemorrhage, space occupying lesion, acute infarct, hydrocephalus or shift of midline structures. A magnetic resonance angiogram showed no vascular abnormality, ruling out a posterior communicating (PCOM) artery aneurysm.

Her laboratory results revealed a rising creatinine level 129 μmol/l and intravascular hemolysis (lactate dehydrogenase level 1,183 U/l, reticulocyte count 3.2 %, decreased haptoglobin <0.10 g/l). Peripheral blood film showed fragmented cells, confirming a diagnosis of hemolysis associated with HELLP syndrome.

A workup for various causes of stroke in a young patient was performed during her ICU stay. Serum levels of rheumatoid factor, C3/4, folate and vitamin B12, lupus anticoagulant, anti-cardiolipin immunoglobulin G antibody, anti-neutrophil cytoplasmic antibody, anti-double stranded deoxyribonucleic acid, and venereal disease research laboratory test were normal.

With normalisation of BP, her diplopia, right eyelid ptosis improved with spontaneous resolution 5 days later. She was discharged 6 days after her admission. A week after her discharge, anti-hypertensives were stopped as her BP was around 90/40 mmHg without medications.

Discussion

We have described a relatively rare complication of third nerve palsy in a pregnant woman who presented with definitive signs of impending eclampsia (hypertension, hyperreflexia, visual disturbances, proteinuria, bibasal lung crepitations, and easy bleeding from intravenous cannulation attempts). Such signs could rapidly progress to a frank eclamptic fit.

Her right eye signs included a right partial ptosis, binocular diplopia, and limited adduction, elevation and depression of the right eye. Had these third nerve palsy signs occurred as a sole feature in the absence of pre-eclampsia, her management would be different, neuroimaging performed and a neurology consult obtained. However, faced with impending eclampsia, the management priorities are the expedient delivery of the baby and placenta (instigator of the physiological derangements) after initial stabilisation of the mother.

Prevention of eclampsia was instituted by a loading dose of IV magnesium, followed by emergent cesarean delivery within 30 min of admission. Cranial MRI was not performed preoperatively as this could not be arranged rapidly after-hours in our center, and would subject the mother to the risk of eclamptic fit and deterioration en-route to the MRI suite in a remote location. The plan was to perform neuroimaging post-cesarean; had an aneurysm or subarachnoid hemorrhage (SAH) be diagnosed, we would have transferred the patient to another hospital with neurosurgical facilities (as this expertise was not available to us). In centers where both obstetric and neurosurgical expertise are available, a cesarean section and craniotomy/clot evacuation (or ventricular drain insertion) could perhaps be performed in the same operation setting. Here, the value of the pre-operative MRI would logically be very important. Conversely, some doctors may choose to perform cesarean first, and endovascular treatment of ruptured aneurysm post-partum [4].

Her cesarean was performed under a general anesthetic (GA) and not a neuraxial blockade due to the anesthetist's high index of suspicion of worsening biochemical indices, and rightly so with a platelet count of 54×10^9/l and HELLP. This was the best option given that she showed signs of coagulopathy, risking epidural/spinal haematomas and problems of managing an epidural catheter in a coagulopathic patient, and timing its removal. If SAH existed, GA has these additional advantages: intubation and securing the airway (safeguarding from a possible deteriorating glascow coma scale (GCS) and inability to protect the airway from aspiration), ability to control ventilation, tidal volumes and respiratory rate and perform hyperventilation to prevent hypercarbia, hypoxia and circumvent cerebral oedema and other secondary brain

injury. So, GA was a reasonable choice for this patient [5].

Postoperatively, stroke and surgical causes of third nerve palsy were ruled out via MRI/MRA scans. Her condition improved with the delivery of the baby, BP control, and magnesium sulphate.

The exact cause of third nerve palsy in preeclampsia remains unclear. It has been postulated that auto-regulatory failure occurs once blood pressure increases and exceeds the upper limit of cerebral autoregulation [6, 7]. This causes hyperperfusion and breakdown of the blood–brain-barrier, with extravasation of fluid/blood into the brain parenchyma. Another postulation is that the disordered cerebral autoregulation leads to focal reactive vasoconstriction, resulting in local hypoperfusion. Endothelial dysfunction may also play a role. These postulated mechanisms are also responsible for hypertensive encephalopathy, eclampsia and posterior leukoencephalopathy syndrome [8].

The commonest cause of a complete, pupil-sparing third nerve palsy is ischaemia [9], whereas in a complete, pupil-involving third nerve palsy, (which our patient had), it is vital to rule out an internal carotid or posterior communicating artery aneurysm.

There are two other documented cases of third nerve palsy during pregnancy [10, 11], and reports of other nerves (facial and abducens) being affected [12–16]. Bonebrake et al. [11] reported a case of third nerve palsy in a woman with simultaneous symptoms of preeclampsia and visual disturbances. Theirs was a 19 year-old primigravida (31 weeks gestation) with no etiology other than pre-eclampsia. She underwent a preterm cesarean delivery for worsening renal function, with complete spontaneous resolution of her third nerve palsy 2 months post-partum.

Watanabe et al. [10] reported a 35-year-old, gravida 4 para 2, (with history of gestational hypertension in two previous pregnancies) with a BP 149/102 mmHg at 13 weeks gestation. She was admitted at 28 + 5 weeks with BP 170/107 mmHg and treated with methyldopa and hydralazine. Preeclampsia was diagnosed at 29 + 6 weeks when proteinuria occurred and dexamethasone commenced at 30 + 3 weeks. Cesarean section was performed at 31 weeks for abruptio placentae, with double vision presenting post-operatively. Ophthalmologic evaluation revealed serous retinal detachment, and left third nerve palsy. MRI/MRA and conventional angiography excluded aneurysms and organic brain lesions.

Prognosis for third nerve palsy in preeclampsia appears to be good, with Bonebrake's case spontaneously recovering 2 months post-partum; Watanabe's and ours in 3 days. Fung et al. [16] found that the common factor in abducens nerve palsy in pregnancy was late gestational hypertension; this holds true for third nerve palsies, after excluding other causes. Spontaneous recovery, no matter how early, still necessitates neuroimaging to exclude aneurysms as visual symptoms caused by them can resolve completely after delivery [17].

In summary, this unusual case of third nerve palsy associated with preeclampsia and HELLP syndrome reminds us that good recovery is possible, provided BP control is achieved and aneurysms are excluded.

Acknowledgments Informed written consent for publication was granted by the patient. The Singhealth Centralised Institutional Review Board committee deemed the study exempt from review [Protocol No. CIRB 2010/409/D].

Conflict of interest The authors have no competing interests.

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