A case of neuropsychiatric effects of pre-eclampsia / eclampsia

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Neurological manifestations of pre-eclampsia and eclampsia are well recognised. The evidence for association between pre-eclampsia / eclampsia, mental health problems and psychotropic medications is developing. Psychiatric disorders and pre-eclampsia / eclampsia are commonly seen clinical problems during pregnancy, and untreated cases can have serious outcomes. The available literature is not able to indicate causal association in any direction. This case report and the related literature review will demonstrate the complex nature of these relationships.

Our case, a 21-year old primiparous single, white-British woman with pregnancy-induced hypertension and pre-eclampsia, was five months postpartum at the time of writing. She delivered a baby girl at 38 weeks gestation. Labour was induced with amniotomy and prostaglandins. She also needed intravenous oxytocin during induction. She sustained a second degree perineal tear during labour. There were no reports of any other delivery or postpartum complications.

The patient had her first antenatal appointment in April 2013 at nine weeks gestation. Her past medical history included tonsillectomy at the age of seven years and allergy to dust mites. There was no past or present intake of alcohol or illicit drugs. She gave a history of diabetes and hypertension in her maternal aunt and maternal grandmother. Her sister had a history of severe pre-eclampsia, progressing to eclampsia with seizures during labour. This necessitated admission to intensive care.

At nine weeks gestation, her weight was 92Kg, BMI 34Kg/m2, and blood pressure 132/82mmHg. Investigations identified low serum B12 (151ng/L – normal range 180-1130ng/L) and folate (2ug/L – normal range 3.0-20.0ug/L) levels. Her glucose tolerance test was reported to be normal in the second and third trimesters. Urine protein level was tested repeatedly and it ranged from 0.3 to 0.5g/L (normal level in pregnancy <0.3g/L), and protein/creatinine ratio 15 to 40mg/mmol (abnormal >45mg/mmol). Her blood pressure ranged from 100/60mmHg earlier in the pregnancy, to a maximum of 147/95mmHg towards later stages of the pregnancy, when she had proteins in her urine consistently. She did not describe any abdominal pain, and physical examination never detected any abdominal tenderness which alongside normal liver enzyme levels excluded haemolysis, elevated enzymes and low platelets (HELLP) syndrome.

The patient was referred to perinatal psychiatry services at 33 weeks gestation by the obstetric team for having visual hallucinations in the form of spiders and people, alongside auditory hallucinations. Due to regrettable fragmentation in services, there was a delay in seeing the patient. When assessed by the perinatal team, the patient reported that since early pregnancy she had been having constant daily headaches, accompanied by ‘gritty feelings’ in her eyes, and experiences of lights and sounds seeming louder and intolerable. She added that since 20 weeks gestation she had seen ‘floaters’ in her peripheral vision. She had seen spiders crawling on her bed and once crawling over her mother in the second trimester of pregnancy, when she was about to sleep. The patient furthermore reported hearing muffled voices, intermittently and lasting only a few seconds. She was not able to make out their content. She experienced insomnia, which was mostly due to pelvic girdle pain. The patient’s social situation was somewhat stressful, and she had intermittent mild anxiety and depressive symptoms at sub-syndromal level. She did not have delusions, bizarre ideations or any other psychotic symptoms apart from the previously mentioned auditory and visual hallucinations. There was no previous history of psychiatric illness. The patient’s sister suffered mild postnatal depression following a traumatic birth...
Pre-eclampsia and eclampsia: general facts
Definitions:
Pre-eclampsia: a multisystem disorder whereby the presence of significant proteinuria is associated with oedema and raised blood pressure during pregnancy; most commonly occurs >20 weeks gestation.
Eclampsia: a complication of pre-eclampsia whereby the patient has one or more generalised seizures.
Proteinuria: ≥0.3g urinary protein excreted within 24 hours.
Based on the National Institute for Health and Care Excellence (NICE) guidelines, the diagnostic criteria for pre-eclampsia involve new onset of hypertension during pregnancy (after 20 weeks gestation) which is based on at least two measurements taken four hours apart alongside the presence of significant proteinuria.
Hypertension severity classification:
Mild: 140/90mmHg – 149/99mmHg
Moderate: 150/100mmHg – 159/109mmHg
Severe: >160/110mmHg
Incidence: pre-eclampsia is a relatively common condition affecting about 5-8% of pregnancies.1
Pathophysiology: pre-eclampsia is increasingly being recognised as a disease entity caused by immune-mediated endothelial damage which results in increased capillary permeability. The immune response may be elicited by release of substances from an inappropriately attached placenta. The placenta is the central organ in the development of pre-eclampsia, as without this the condition would not exist. In a normal placentation, trophoblastic cells from the anchoring villi of the foetal placenta invade the maternal endothelium and acquire an endothelial form, which causes vessels to become leaky thus allowing maternal blood to fill intravenous spaces of the placenta. In preeclampsia, fewer trophoblastic cells move into the maternal endothelium, causing the vessels to become constricted and highly resistant which therefore deprives the placenta of oxygen. This hypoxia alongside other factors results in the symptoms of pre-eclampsia.2
Risk factors for pre-eclampsia: first pregnancy, family history, age above 40 years, previous history of pre-eclampsia and carrying twins or multiple pregnancies. And short stature.
Clinical features: Early signs of pre-eclampsia are raised blood pressure, pedal oedema and proteinuria. Symptoms can include severe headaches, visual problems, eg seeing flashes of light, fluid retention, weight gain and vomiting. Pre-eclampsia can lead to several complications such as eclampsia, HELLP syndrome, stroke, disseminated intravascular coagulation, multi-organ failure, foetal growth retardation and, in rare cases, maternal and/or foetal death.3
Treatment: Low dose aspirin is used to prevent the condition in high risk cases or for treatment in early stages. Antihypertensive medications, eg labetalol, methyldopa and nifedipine can be used for controlling hypertension. Magnesium sulphate and anticonvulsants are used when eclampsia has developed. Delivering the baby early can reduce the risk of complications, hence induction of labour after 37 weeks or caesarean section is recommended.1
Due to eclampsia. Mental state examination was normal, including cognitive functioning.
A full neurological examination was carried out: no focal or generalised abnormalities were detected. We did not offer the patient psychotropic medication, although it was planned to give low dose quetiapine if the hallucinations began to affect her in any significant way, or posed any risk issues.
Following induction of labour, the patient was monitored for changes in psychopathology. The patient reported that all her symptoms had resolved since the delivery when she was seen by services 72 hours later and remained asymptomatic thereafter. There were no reports of headaches, visual disturbances, hallucinations, stress or insomnia. She cared for her infant adequately, and no signs or symptoms of anxiety or depression were observed. She was discharged from psychiatric services three months after delivery.
Discussion
This case raised an interesting diagnostic challenge. The patient clearly had hallucinatory experiences and insomnia as primary mental health symptoms. There were accompanying physical symptoms like pelvic girdle pain as well as headaches and visual disturbances indicating the possibility of pre-eclampsia. The provisional diagnosis of the psychiatric team was that although the patient had subsyndromal mixed anxiety and depression, her hallucinatory experiences were best explained by pre-eclampsia. Emergence of symptoms during later stages of pregnancy, borderline hypertension, proteinuria, and most importantly, rapid resolution of symptoms after delivery, indicates that the most likely explanation of her symptoms was pre-eclampsia. The clinical picture did not fit well with typical functional psychiatric illness presentations.
Neurological manifestations of preeclampsia include headaches, hyper-reflexia, visual changes and blindness. In a series of eight cases with eclampsia Chakravarty and Chakrabarti reported that all of them had seizures, altered senso- rium and retinal artery spasm on fundoscopic examination.4 Six had holocranial headaches and five had blurred vision. CT scans in seven cases showed bilateral hypodense occipital lesions involving more white than grey
matter. In five patients these lesions extended to parietotemporal areas. Hypodense areas tended to have hyperdense centres, suggesting haemorrhage in the centre. The sensorium improved after 36-48 hours and blurred vision after seven days. All patients were clinically asymptomatic at three-four months follow-up, with complete resolution of CT scan changes in all.

In another study (n=39: pre-eclampsia n=30 and eclampsia n=9) MR imaging was abnormal in 18 patients. The occipital lobe was involved in all patients, followed by the parietal, frontal, and temporal lobes, basal ganglia and pons. In other case reports, changes in eclampsia have been described as posterior reversible encephalopathy syndrome (PRES). It is a clinical-radiological syndrome with symptoms of headache, vomiting, epileptic seizures, visual disorders and altered level of consciousness, associated with lesions mainly located in the white matter of the posterior regions of the brain.

The pathophysiological mechanisms by which neurological symptoms and complications arise in eclampsia have been studied and supported by cerebral changes on CT / MRI. In normal physiology, constant cerebral blood flow (CBF) is maintained during changes in circulation by the brain’s autoregulation system whereby cerebral resistant vessels constrict with high blood pressure and dilate with low blood pressure. In eclampsia, there is constant high systolic pressure or a sudden increase in mean arterial pressure, which impairs vascular autoregulation causing extravasation of fluid and increased CBF producing focal hydrostatic cerebral oedema. Contributing factors to this oedema also include, pressure-induced vasodilatation in cortical areas and loss of vasoconstriction mainly in posterior areas of the brain.

**Psychiatric aspects**

Psychiatric symptoms generally manifest when eclampsia develops, and include visual hallucinations. The mechanism by which visual hallucinations arise has been addressed in the literature. The presence of lesions, leads to deafferentation of the visual system and causes cortical release phenomenon. Deafferentation effectively moves normal inhibitory processes and the deafferentated neurones undergo specific molecular and biochemical changes that overall increase in excitability causing visual hallucinations.

Eclamptic psychosis has been described in the literature but to the best of our knowledge there are no reports of psychosis in pre-eclampsia. In a recent case-report progression of eclampsia to florid puerperal psychosis with hallucinations, delusions and bizarre behaviour has been described. The psychosis only responded to electroconvulsive therapy, after failure of pharmacological treatment.

**Depression and antidepressive treatment**

The patient had subsyndromal mixed anxiety and depression and her sister had eclampsia and postnatal depression, which makes it pertinent to discuss relationship of depression, antidepressants and pre-eclampsia / eclampsia in this report.

The association between depression, antidepressant treatment, and subsequent pre-eclampsia is complex. In a case-controlled study of 339 pre-eclamptic cases and 337 normotensive controls, the prevalence of moderate depression was 11.5% among cases and 5.3% among controls, whereas the prevalence of moderate-to-severe depression was 3.5% for cases and 2.1% for controls. Compared with non-depressed women, those with moderate depression had a 2.3 fold increased risk of pre-eclampsia (95% CI: 1.2-4.4), while moderate-to-severe depression was associated with a 3.2-fold (95% CI: 1.1-9.6) increased risk of pre-eclampsia.

In a case register-based study pre-eclampsia prevalence was reported to be higher amongst depressed pregnant patients treated with antidepressants compared with untreated depressed pregnant patients (adjusted relative risks of 1.22, 1.95 and 3.23 for SSRIs, SNRIs and TCAs respectively). It is not clear if these associations reflect causal effects of antidepressants or depression in the aetiology of pre-eclampsia, as the possibility remains that antidepressant continuers have higher severity of depression than those who stop taking the drugs, thus antidepressant use is a confounding variable in this association.

**Conclusion**

Both pre-eclampsia and depression are common conditions in pregnancy, with a possibility of serious outcomes if not treated adequately. The association of pre-eclampsia with depression may indicate a common endothelial or vascular aetiology for these disorders.

There may be a possible association of antidepressant use (mainly SNRIs and TCAs) with pre-eclampsia but these associations may be reflecting an effect of the severity of depression, rather than drug effects per se.

Reversible occipital lobe lesions can be seen on MRI scan in eclampsia and some cases of pre-eclampsia. These lesions give rise to visual changes and
visual hallucinations during the pregnancy.

Eclamptic psychosis has been recognised, and may mimic or manifest as puerperal psychosis.

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References