

SHORT REPORT

Late onset postpartum eclampsia without pre-eclamptic prodromi: clinical and neuroradiological presentation in two patients

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Abstract

In two patients eclampsia started 9 days postpartum. Headache and visual disturbances preceded seizures but none of the classic pre-eclamptic signs oedema, proteinuria, and hypertension were present until shortly before seizure onset. Brain herniation (patient 1) and status epilepticus (patient 2) necessitated neurointensive care management. Brain MRI initially showed only frontal sulcal effacement in one patient but later showed white matter hyperintensities on T2 weighted images and a previously undescribed pattern of cortical-subcortical postgadolinium enhancement on T1 weighted images in both. Neurological deficits and MRI findings were reversed with therapy in both patients. It is concluded that late postpartum eclampsia can manifest without classic prodromi and that characteristic MRI findings may lag behind clinical manifestation.

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Eclampsia continues to be a poorly understood neurological complication of pregnancy that substantially contributes to maternal morbidity and mortality. Its classic clinical presentation consists of epileptic seizures or coma manifesting during the third trimester or early puerperium in women who already have the pre-eclamptic symptom triad of oedema, proteinuria, and hypertension.¹ The diagnosis of eclampsia also requires the exclusion of other medical or neurological disorders underlying the symptomatology.

The previously controversial existence of a delayed postpartum variant of eclampsia is now acknowledged by most experts.^{2,3} Unusual timing, however, may not be the only feature of late onset postpartum eclampsia (LPE) deviating from the above classic diagnostic criteria of eclampsia. In a case series of patients with LPE, Lubarsky *et al*² reported that a substantial subset of women diagnosed with LPE had not been identified as pre-eclamptic before seizure onset. It remained unclear whether this repre-

sented a true variant of the clinical presentation of eclampsia or merely reflected decreased caretaker attention towards pre-eclamptic signs in the postpartum period.

Obviously, the combination of delayed manifestation after delivery and an atypical clinical presentation can pose a diagnostic challenge. Several recent case series of classic eclampsia as well as LPE reported characteristic findings on brain MRI⁴⁻⁹ consisting of mostly reversible, white matter hyperintensities on T2 weighted images. Consequently, MRI has been proposed as a highly sensitive adjunctive test for eclampsia, especially in atypical or severe cases.

We report the clinical and neuroradiological course of life threatening LPE in two patients in whom seizures manifested without a preceding pre-eclamptic phase. Brain MRI failed to show characteristic findings in one patient early on. Later, however, MRI showed findings characteristic of eclampsia as well as a previously undescribed pattern of contrast enhancement.

Case reports

PATIENT 1

A 28 year old healthy black woman (gravida four, para two) delivered a healthy girl in pregnancy week 41. Puerperium was normal without oedema, proteinuria, or hypertension until the 9th postpartum night (day 1) when she gradually developed severe headache accompanied by vomiting and flickering visual scotomata. As her blood pressure was 190/120 mm Hg on hospital admission, she was treated with nifedipin. She was alert and oriented, with moderate neck stiffness but no focal neurological signs. Initial cranial CT was normal. Analysis of CSF showed 5×10^4 erythrocytes mm^{-3} and $11/\text{mm}^3$ white blood cells; CSF protein was 168 mg/dl, CSF glucose 37 mg/dl. Four vessel intra-arterial cerebral angiography after transfer to our hospital was normal except for minor vessel irregularities in one branch of the left middle cerebral artery. The next day she experienced three generalised tonic-clonic seizures. Intravenous phenytoin was started. At night she became comatose and was intubated. Her left pupil was dilated and sluggishly reactive to light. Deep tendon reflexes were brisk. T2 weighted images showed multiple areas of

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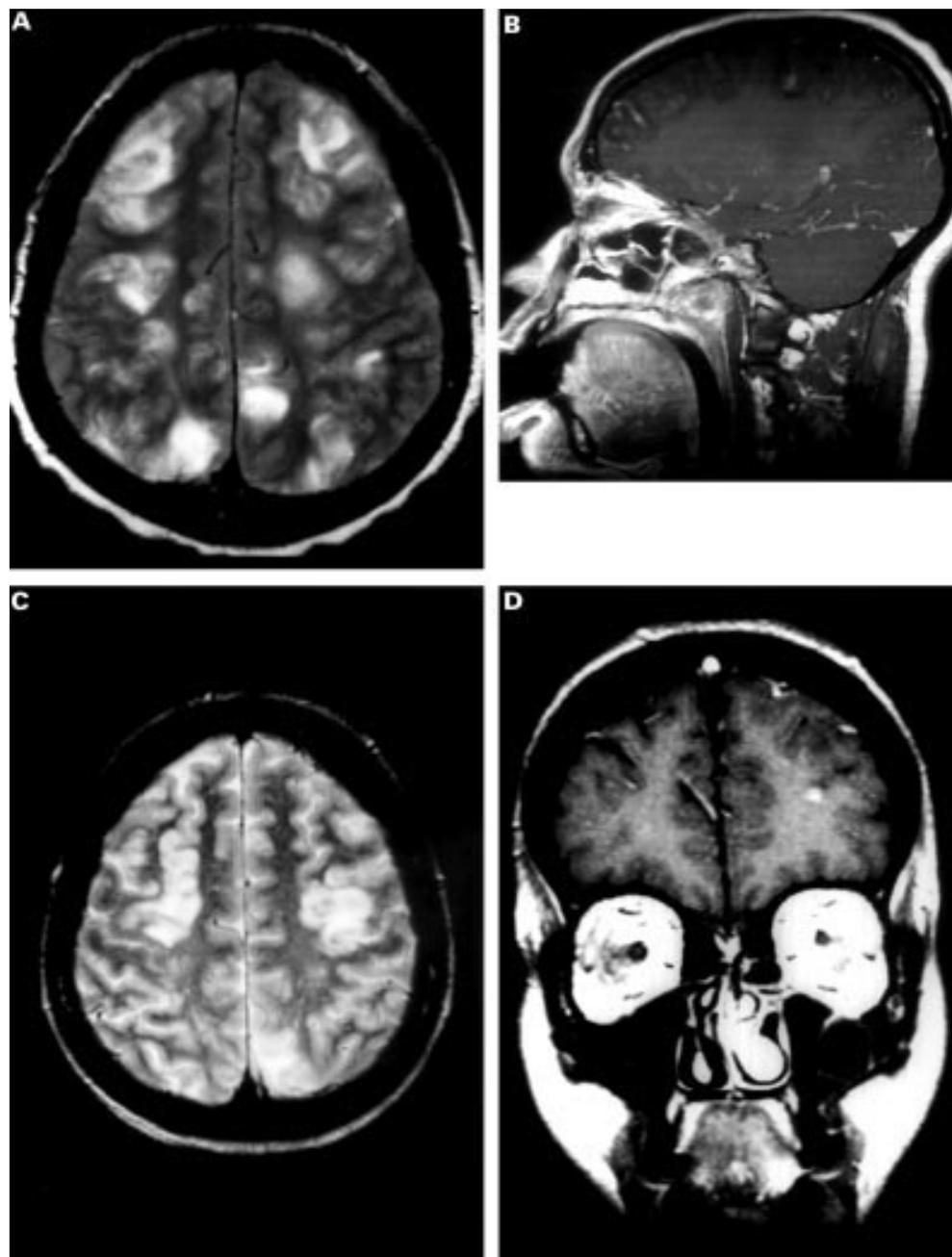


Figure (A) Axial T2 weighted MRI (patient 1) shows characteristic areas of hyperintense signal in the occipital, frontal, and parietal lobes bilaterally. Multifocal hyperintensities are primarily located in the cortex and adjacent subcortex. They are patchy or follow the course of the gyri in a serpiginous fashion. On follow up MRI, these hyperintensities were completely reversible. (B) Sagittal postgadolinium T1 weighted MRI (patient 1) shows prominent streaky enhancement of pial vessels in cortical sulci and multifocal patchy enhancement in the frontal and parietal cortex. Note that the cortex appears oedematous in some areas of prominent vascular and patchy parenchymal enhancement. (C) Axial T2 weighted MRI (patient 2). Characteristic hyperintense foci in the left occipital and bilateral frontoparietal lobes. The hyperintense areas follow the cortical gyri and extend into the subcortical white matter. (D) Coronal postgadolinium T1 weighted MRI (patient 2). Patchy corticosubcortical enhancement in the left frontal medial gyrus in addition to vascular enhancement.

hyperintense signal in the cortex, the white matter, and along the cortical-subcortical junction of the occipital, parietal, temporal, and frontal lobe (figure A) and in both cerebellar hemispheres. Only some of these areas were hypointense on corresponding T1 weighted images. Postgadolinium-DTPA T1 weighted MRI demonstrated pial vascular enhancement and patchy enhancement in the oedematous cortex and adjacent subcortex (figure B). Multifocal, predominantly supratentorial, oedema caused transtentorial herniation.

Therapy for increased intracranial pressure was initiated (hyperventilation, head elevation, intravenous mannitol, tris-hydroxy-methyl aminomethane, methohexital, ventricular drainage). Pupillary diameters became equal again. Follow up MRI (day 10) showed a decrease of hyperintense areas. After sedation and muscle relaxation were discontinued, she slowly regained consciousness and was extubated. Transiently, she remained disorientated and agitated but 3 weeks later she was discharged without neurological sequelae. Cor-

respondingly, MRI had become normal. Follow up neurological examination and EEG 8 months later were normal.

PATIENT 2

A 38 year old healthy white woman (gravida one, para one) delivered a healthy girl by caesarean section after arrest of labour. The postoperative course during her hospital stay was normal until the 9th day postpartum when she complained of a rapidly developing headache and bright visual scotomata. Whereas blood pressure measurement earlier the same day had yielded 130/80 mm Hg, blood pressure was 170/100 mm Hg then and nifedipine was started. One hour after symptom onset she had a generalised tonic-clonic seizure. Initial cranial CT was normal. Lumbar puncture showed two white blood cells/mm³ and CSF protein of 95 mg/dl. Although intravenous phenytoin was initiated, she experienced four generalised tonic-clonic seizures during the next 36 hours. Brain MRI without contrast 15 hours after symptom onset only disclosed effacement of the left superior frontal sulcus on T1 weighted images. On referral to our institution (day 4) she seemed somnolent, but focal neurological signs were absent. Antihypertensive therapy was switched to dihydralazine. She developed a convulsive status epilepticus which could not be controlled by increasing intravenous phenytoin, magnesium sulfate, and diazepam. After intubation she received thiopental resulting in EEG burst suppression. Follow up T2 weighted images on day 4 showed hyperintense lesions involving the cortex, and the white matter including the grey-white matter junction in parts of the superior and medial frontal gyri, the precentral gyri, in parieto-occipital areas, and both cerebellar hemispheres (figure C). Post gadolinium-DTPA T1 weighted images showed prominent enhancement of pial vessels in the area of the superior and medial frontal gyri bilaterally. Contrast enhancement was also present within the parenchyma of the left frontal medial gyrus (figure D). Repeated CSF examination showed 16 383 erythrocytes/mm³, 14/mm³ white blood cells, and protein of 99 mg/dl. Four vessel cerebral intra-arterial angiography was normal. After thiopental was discontinued the next day, she gradually regained consciousness but transient optical and acoustical hallucinations developed. Follow up MRI on day 26 showed only slight residual effacement of the frontal superior sulci bilaterally and a few punctate hyperintensities in the parieto-occipital white matter on T2 weighted images. Postgadolinium T1 weighted images showed no contrast enhancement within the parenchyma and no prominent vascular enhancement.

Discussion

Our diagnosis of eclampsia was based on the clinical and neuroradiological course and the exclusion of other underlying disorders in both patients. Our differential diagnostic considerations included sinus/cerebral vein thrombosis and subarachnoid haemorrhage from an aneurysm, which were ruled out by cerebral

angiograms. Infectious/autoimmune-inflammatory disorders were unlikely because of the clinical course, negative findings on multiple blood and CSF cultures, no significant increase in CSF white blood cells, and numerous negative serological studies. Sick cell crisis, which can produce similar signs on MRI, was excluded by haemoglobin chromatography in patient 1.

Thus, the presented cases are important clinical and neuroradiological variants of eclampsia. Firstly, eclampsia started on the 9th postpartum day in both patients. Although such delayed manifestation of eclampsia was controversial in the past, the existence of a late onset postpartum variant of eclampsia is now generally accepted.^{2,3} Strikingly, no pre-eclamptic signs were noted in our patients until postpartum day 9, when hypertension started acutely. This corresponds to findings by Lubarsky *et al*⁵ who reported that 44% of their patients with LPE had not been identified as pre-eclamptic before seizure onset. These authors, however, did not comment on whether pre-eclamptic signs were truly absent or were not identified due to insufficient caretaker attention towards pre-eclampsia during the postpartum period. Particularly in our second patient, who remained in hospital after a caesarean section, daily examination including blood pressure measurements disclosed normal values even until shortly before seizure onset. Our findings therefore demonstrate that the classic pre-eclamptic signs of oedema, proteinuria, and hypertension do not evolve before seizure onset in some patients with LPE—a constellation that may be referred to as “eclampsia without pre-eclampsia”. Instead of classic pre-eclamptic signs, both of our patients complained of severe headache accompanied by visual disturbances during the hours before seizure manifestation. Presence of these prodromal symptoms in postpartum women even in the absence of preceding oedema, proteinuria, and hypertension, should cast suspicion on impending eclampsia.

Recent case series^{4,9} stressed the presence of “characteristic” MRI findings in eclampsia which may partially represent vasogenic oedema.¹⁰ Conversely, however, the potential absence of “characteristic” findings, which may lead to false dismissal of the diagnosis, has not received much attention. The initial MRI in our second patient showed only unilateral frontal sulcal effacement. Only later MRIs yielded “characteristic” multiple hyperintensities on T2 weighted images in the cortex, white matter, and adjacent to the grey-white matter junction. So far, only two eclamptic patients with normal MRI have been reported.^{4,5} In both, a single epileptic seizure and headache were the only neurological manifestations. Brain MRI was obtained only 5 days after the seizure in one patient and no follow up scans were available in either case.^{4,5} By contrast, our findings prove for the first time that “characteristic” MRI findings may lag behind seizure manifestation and that absence of these findings does not necessarily indicate a mild clinical course.

In our patients, contrast enhanced MRI showed evidence of a transient impairment of the blood-brain barrier in the oedematous cortex in addition to pial vascular enhancement. Recovery of integrity of the blood-brain barrier preceded or paralleled the regression of oedematous foci and clinical improvement. Post-contrast enhancement in eclampsia has so far only been reported by Digre *et al*⁴ in one patient. The cortical enhancement in our patients (figure B) is a different, highly unusual pattern which represents a so far unidentified MRI correlate of eclampsia. However, similar enhancement has been described in encephalopathy induced by cyclosporin.¹¹ Moreover, postcontrast MRI findings and evidence for impairment of the blood-CSF barrier on CSF analysis on the one hand, and largely normal cerebral angiographies on the other hand, suggest that the cerebral microcirculation, not the macrocirculation, is the primary target of eclampsia. Conceivably, eclampsia shares this final pathophysiological pathway with diverse other disorders (for example, hypertensive encephalopathy, cyclosporin toxicity) leading to a so called predominantly “posterior leukoencephalopathy syndrome” on MRI.⁹

We conclude that late onset postpartum eclampsia can manifest without a preceding preeclamptic phase and instead solely acute severe headache and visual disturbances may

herald impending eclampsia in such patients. Although MRI is an important diagnostic test in atypical or severe eclampsia, it may fail to show “characteristic” findings early after onset of eclamptic seizures. Finally, we report a previously unidentified pattern of cortical post-contrast enhancement on MRI in LPE.

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