

REVERSIBLE POSTERIOR LEUKO-ENCEPHALOPATHY SYNDROME: A CASE REPORT

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SUMMARY

In a patient who was hospitalized for acute illness, we have noted a syndrome of altered mental functioning, seizures, severe hypertension and renal dysfunction, with findings indicating predominantly posterior leukoencephalopathy on brain CT scan. The findings on brain CT scan are characteristic of subcortical edema without infarction and are reversible. The patient was treated with anti-hypertensive medications and the neurological deficits recovered completely within thirteen days. Follow-up CT scan showed resolution of abnormalities in ten days. A diagnosis of reversible posterior leukoencephalopathy syndrome was made retrospectively; we decided to report this case as we have noted that many physicians and radiologists are unaware of this relatively recently recognized neurological disorder, which has a good outcome with early diagnosis and prompt management.

KEY WORDS: Leukoencephalopathy, Hypertensive encephalopathy, Glomerulosclerosis

Pak J Med Sci April-June 2005 Vol. 21 No. 2 213-6

INTRODUCTION

Reversible Posterior Leukoencephalopathy Syndrome {RPLS} is a recently recognized syndrome. It was first described in 1996 when Hinchey et al. in a retrospective study noted white matter edema on neuroimaging in the posterior temporo-parieto-occipital regions in

a variety of conditions, including severe hypertension, toxemia of pregnancy, use of immunosuppressive and cytotoxic agents. They proposed the name RPLS emphasizing its location and relatively reversible nature¹.

A 1996 study of 15 patients in Europe and the United States with this syndrome listed the most common clinical features as headache, altered alertness and behavior, seizures and abnormalities of visual perception¹. A review of 52 cases of RPLS in the pediatric population confirmed these four signs and symptoms as being the most common^{1,2}. Radiologically, extensive bilateral white matter abnormalities suggestive of edema in the posterior regions of cerebral hemispheres are seen³. Essentially, the diagnosis of RPLS is retrospectively, significant reversal of neuroradiological abnormalities coupled with complete clinical recovery suggest the diagnosis⁴. The recognition of the syndrome is critical as delay in the diagnosis or treatment can result in permanent neurological deficits while prompt early control of blood pressure or withdrawal of causative drugs can reverse the syndrome⁵.

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* Received for publication: January 13, 2005

Accepted: March 28, 2005

CASE REPORT

A 23-year-old Indian, male patient was brought to casualty in a state of coma with a history of a witnessed generalized tonic-clonic seizure at home. On examination, the patient was comatose with Glasgow coma scale 7/15. Vital signs revealed: pulse = 100 bpm, temperature = 36.8°C, respiratory rate = 18 / min, blood pressure = 300/120 mmHg, O₂ saturation 94% on room air by pulse oximetry. There was puffiness of the face and mild pallor. Neurological examination revealed a comatose patient with no signs of meningeal irritation, normal fundus examination and evidence of pyramidal affection in the form of hypertonia, brisk deep tendon jerks and bilateral sustained ankle clonus with bilateral extensor plantar response. Examination of the cardiorespiratory system and abdomen was otherwise unremarkable.

During examination, the patient sustained a generalized tonic-clonic convulsion, which was aborted with parenteral diazepam, following which he was intubated and shifted to the intensive care unit.

Investigations: CBC: WBC = 12 X 10⁹/l, Hb = 10.3 g/dl, platelet = 214 X 10⁹/l, MCV = 80.4 fl, MCH = 29.1 pg, ESR = 27 mm/hr.

Biochemical profile: Blood sugar = 8.4 mmol/l, blood urea = 16.9 mmol/l [RR: 2.5-6.6 mmol/l], S. creatinine = 386 µmol/l [RR: 60-120 µmol/l], S. potassium = 4.6 mEq/l [RR: 3.5-5.0], S. sodium = 138 mEq/l [RR: 135-145], S. albumin = 19g/l [RR: 37 - 47 g/l], S. Total protein = 4.8g/l [RR: 60-83g/l], total cholesterol = 7.2 mmol/l [RR: 3.5-5.4], S. triglyceride = 5.3 mmol/l, pH = 7.31, S. HCO₃ = 16 mmol/l, PaO₂ = 12 Kpa, PaCO₂ = 5.2 Kpa. Other laboratory profile including S. calcium, magnesium, phosphorus, hepatic and coagulation profile were normal. Urine routine showed dysmorphic red cells, red cell casts and +++ proteins, 24 hour urine proteins = 3675 mg/24 hrs, creatinine clearance = 0.13 ml/s [RR: 1.5-2.3 ml/s].

Ultrasound revealed normal kidney size and echotexture. Renal biopsy subsequently carried

out revealed focal segmental glomerulosclerosis. S. Complement level was normal, collagen screen was negative, ASOT < 200 IU/ml, complete sepsis work-up including urine C & S, blood C & S, thin and thick blood film for malaria, tuberculin test, VDRL, HIV 1/2, serology for echinococcosis and toxoplasmosis were negative. Lumbar puncture revealed a normal CSF study.

Plain brain CT revealed bilateral symmetrical hypodensities in the white matter of posterior parieto-occipital regions with no mass effect or midline shift [Fig. 1a,b].

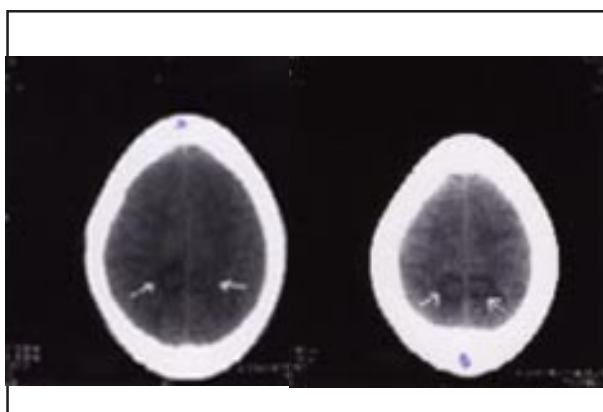


Figure 1 a, b: Non-contrast Cranial CT scan showing bilateral posterior parieto-occipital white matter hypodensities.

Management

Anti-hypertensive medications were immediately started in the form of sodium nitropruside along with parenteral phenytoin 300mg/day, intravenous mannitol 20% 100cc three times per day and parenteral ceftriaxone 2g twice/day. His blood pressure ranged from 160--180 mmHg systolic and 90-100 mmHg diastolic. On 3rd day of hospitalization, the patient was extubated and neuro-physical re-evaluation revealed an altered mental status in the form of mild confusion with reduced spontaneity of speech; pupils reacted normally to light with normal fundus examination; generalized weakness of pyramidal nature grade III-IV with brisk deep tendon jerks, bilateral sustained ankle clonus and bilateral extensor plantar response. On 7th day, the patient was shifted to the medical ward, anti-hypertensive medications were intensified and the patient became normotensive [blood pressure = 135/

85 mmHg]. On the 10th hospital day, a follow-up plain brain CT revealed resolving hypodensities [Fig: 2a,b].

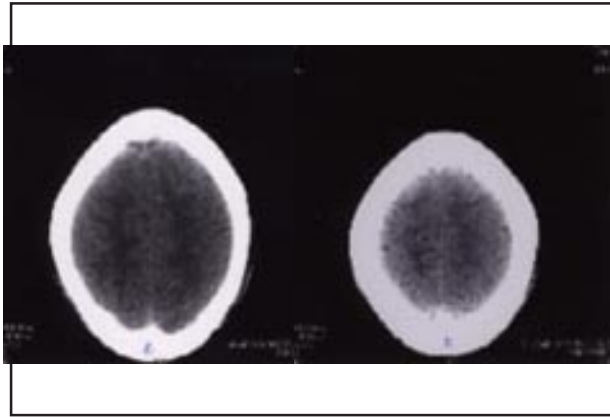


Figure 2 a, b: Follow-up non-contrast Cranial CT scan showing resolving hypodensities.

On thirteenth day, there was complete recovery of the neurological deficits. The patient was discharged on steroid therapy for his renal problem and anti-hypertensive medications. On follow-up, his proteinuria had partially responded [1.3 g/day], his renal function remained stable [S. creatinine = 350 μ mol/l, blood urea = 17 mmol/l] and he had no recurrence of seizures.

DISCUSSION

RPLS may occur in a host of clinical situations such as toxemia of pregnancy^{6,7}, chemotherapy⁸, hypertensive encephalopathy⁹⁻¹², erythropoietin therapy¹³, thrombotic thrombocytopenic purpura¹⁴, acute intermittent porphyrias¹⁵, following organ transplantation¹⁶, collagen vascular disorders such as systemic lupus erythematosus, polyarteritis nodosa, Behcet's disease and acquired immunodeficiency syndrome¹⁷. However, hypertensive encephalopathy, toxemia of pregnancy, cyclosporine A toxicity and uremic encephalopathy are the most common causes of RPLS¹⁸.

The unifying cause of the neurological disorder in these conditions is disturbed arterial cerebrovascular auto-regulation leading to extravasation of fluid into the brain parenchyma. The vulnerability of the posterior circulation may be explained by the paucity of autonomic innervation as compared to the anterior circula-

tion. The resulting edema is usually vasogenic and reversible but may become cytotoxic in some patients¹⁹.

Hypertension of renal origin has been reported to be a significant cause of RPLS accounting for over 25% of cases in one study in both children and adult patients¹². Patients with renal dysfunction seem to be at higher risk for developing RPLS despite only moderate acute elevation of their blood pressure¹⁰. As in our patient, Hinchey et al.¹ reported four patients with RPLS associated with renal disease (one with glomerulonephritis, one with acetaminophen induced hepato-renal syndrome and two with lupus nephritis). The patients were treated with anti-hypertensive medications, and in all patients the neurological deficits resolved within two weeks. Again in correlation with our patient, the syndrome of RPLS can manifest by acute seizures without an obvious prodrome. These patients become seizure-free after resolution of the imaging abnormalities and they do not require long-term anti-epileptic therapy^{9,10}. Another similarity reported, as in our patient is that the fundus examination may be normal (especially in eclampsia patients and patients with renal failure) and pupillary responses are often normal. The deep tendon reflexes are frequently brisk and plantar response may be extensor. A few patients may have weakness and incoordination of the limbs^{1,9,10}.

The findings on neuroimaging in RPLS include non-enhancing white matter abnormalities that appear as areas of low attenuation on CT scan and appear hypo-intense on T₁-weighted imaging MRI and hyper-intense on T₂-weighted imaging MRI. The lesions are mainly seen in the posterior regions of the cerebral hemispheres^{12,19}. These abnormalities partially or completely resolve on follow-up scanning thereby suggesting subcortical edema without infarction. Occasionally, the clinical features and CT scan or standard MRI findings may be indistinguishable from bilateral posterior cerebral artery stroke syndrome. In such patients, the newer MRI techniques [echoplanar Diffusion Weighted Imaging (DWI) and

Apparent Diffusion Coefficient (ADC) maps help in differentiating RPLS from bilateral PCA stroke syndrome. The acutely infarcted areas of the brain are visualized as hyper-intense signals on DWI and hypo-intense signals on ADC maps compared with normal brain tissue¹⁰. Although MRI yields higher resolution and may show focal abnormalities beyond resolution of CT, it is not mandatory for diagnosis of RPLS¹. If the history of an acute seizure or uncontrolled hypertension is not obtained or there is an under emphasized aspect of the clinical presentation and not mentioned to the radiologist, an incorrect diagnosis such as gliomatosis cerebri, progressive multifocal leukoencephalopathy, demyelinating disease or infection may be advised on the basis of neuroimaging. This may result in invasive biopsies or therapies¹⁶.

It is recommended that when high signal intensity in the parietal white matter is seen on MRI and there is a history of seizure or high blood pressure; such patients require a follow-up scan in a period of 1-2 weeks which will most often document the reversibility of the vasogenic edema and avoid expensive or potentially invasive work-ups for other primary cerebral diseases²⁰. The extent of combined T2 and DWI signal abnormalities correlate with the patient outcome. High DWI signal intensity and pseudonormalized ADC values are associated with cerebral infarction and may represent the earliest signs of non-reversibility as severe vasogenic edema progresses to cytotoxic edema²¹.

CONCLUSION

Clinicians must be aware of this syndrome as an early recognition obviates unnecessary diagnostic procedures. Moreover, the syndrome is reversible with prompt treatment and has a good outcome.

REFERENCES

1. Hinchey J, Chaves C, Appignani B et al. A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996; 334:494-500.
2. Soyulu A, Kavukcu, Turkmen M, Akbas Y. Posterior leukoencephalopathy syndrome in post-streptococcal acute glomerulo-nephritis. *Pediatr Nephrol* 2001; 16:601-3.
3. Pavalakis SG, Frank Y, Chusid R. Hypertensive encephalopathy, reversible occipitoparietal encephalopathy, or reversible posterior leukoencephalopathy. Three names for an old syndrome. *J Child Neurol* 1999; 14:277-81.
4. Schwart ZRB, Jones KM, Kalina P et al. Hypertensive encephalopathy. Findings in CT or MRI imaging and SPECT imaging in 14 cases. *Am J Roentgenol* 1995; 159:379-83.
5. Dillon WP. The reversible posterior cerebral edema syndrome. *Am J Neuroradiol* 1998; 19:415.
6. Crawford S, Varner MW, Digre KB, Servais G, Corbett JJ. Cranial magnetic resonance imaging in eclampsia. *Obstet Gynecol*, 1987; 70:474-7.
7. Aneesh B, Singhal MD. Post partum angiopathy with reversible posterior leukoencephalopathy syndrome. *Arch Neurol* 2004; 61:411-6.
8. Small S1, Fukui MB, BramuettGT, Eidelman BH. Immuno suppression induced leukoencephalopathy from tacrolimus (FK 506). *Ann Neurol* 1996; 40: 575-80.
9. Bakshi R, Bates VE, Mechtler LL, Kinkel PR, Kinkel WR. Occipital lobe seizures as the major clinical manifestation of reversible posterior leukoencephalopathy syndrome. Magnetic resonance imaging findings. *Epilepsia* 1998; 39:295-9.
10. Ay H, Buonanno FS, Schaefer PW et al. Posterior leukoencephalopathy without severe hypertension, Utility of diffusion-weighted magnetic resonance imaging. *Neurology* 1998; 51:1369-76.
11. Binsdale H. Hypertensive encephalopathy. *Neurol Clin* 1983; 1:3-15.
12. Hauser RA, Lacey M, Knight MR. Hypertensive encephalopathy. Magnetic imaging. Demonstration of reversible cortical and white matter lesions. *Arch Neurol* 1988; 45:1078-83.
13. Delanty N, Vaughan C, Frucht S, Stubgen P. Erythropoietin associated hypertensive posterior leukoencephalopathy. *Neurology* 1997; 49:686-9.
14. Bakshi R, Shaikh ZA, Bates VE, Kinkel PR. Thrombotic thrombocytopenic purpura. Brain CT and MRI findings in 12 cases. *Neurology* 1999; 52:1285-8.
15. Kupferschmidt H, Bont A, Schnorf H et al. Transient cortical blindness and bioccipital brain lesions in two patients with acute intermittent porphyria. *Ann Intern Med* 1995; 123:598-600.
16. Stein DP, Lederman RJ, Vogt DP et al. Neurological complications following liver transplantation. *Ann Neurol* 1992; 31:644-9.
17. Garg RK. Posterior leukoencephalopathy Syndrome. *Postgrad Med J* 2001; 77:24-5.
18. Casey SO, Sampaio RC, Michel E, Truit CL. Posterior reversible leukoencephalopathy syndrome. Utility of fluid attenuated inversion recovery magnetic resonance imaging in the detection of cortical and subcortical lesions. *Am J Neuroradiol* 2000; 21:1199-1208.
19. Hotermans C, Bottin P, Sodzot B et al. Le syndrome de leukoencephalopathie posterieure reversible. *Revue Medicule de Liege* 2003; 58:472-8.
20. Adam HP, Brott TG, Crowell RM, et al. Guidelines for the management of patients with acute ischemic stroke. *Stroke* 1994; 25:1901-14.
21. Diego J Covarrubias, Patrick H, Luetermer and Norbert G Campeau. Reversible posterior leukoencephalopathy: Prognostic utility of quantitative diffusion-weighted MR images. *Am J Neuroradiol* 2002; 23:1038-48.