Case Report

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

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 common¹². 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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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 comatosed 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 comatosed patient with no signs of meningeal irritation, normal fundus examination and evidence of pyramidal affection in the form of hypertension, 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].

Management

Anti-hypertensive medications were immediately started in the form of sodium nitroprusside 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 reevaluation 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].

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 µmol/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 pregnancy6,7, chemotherapy8, hypertensive encephalopathy9-12, erythropoietin therapy13, thrombotic thrombocytopenic purpura14, acute intermittent porphyries15, 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 circulation. 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 therapy9,10. 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 limbs1,9,10.

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 hemispheres12,19. 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 [echo-planar 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 tissue. Although MRI yields higher resolution and may show focal abnormalities beyond resolution of CT, it is not mandatory for diagnosis of RPLS. 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 therapies.

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 diseases. 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 edema.

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