

# Lupus Nephritis: Viewing Kidneys Through Retinal Periscope

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## ABSTRACT

Hypertensive emergencies are rare in children and mostly attributable to some underlying disorder (secondary) rather than primary hypertension- renal disease being the most common cause. The child can have variable presentation depending on the target organ involved. Unlike benign hypertension, this requires simultaneous management and evaluation in a multidisciplinary approach. We report a case of a 16-year-old girl with complaints of acute onset blurring of vision and headache and diagnosed as Lupus nephritis presenting as hypertensive emergency. This case reiterates the importance of the extensive evaluation which is needed in such cases. Early intervention tends to drastically improve the clinical outcome, since such cases usually have a worse prognosis than their adult counterparts.

**KEYWORDS:** Chronic kidney disease; Hypertensive emergency; Hypertensive retinopathy; Lupus nephritis; SLE; Systemic lupus erythematosus

**ABBREVIATIONS:** ANA: Anti-Nuclear Antibody; BP: Blood Pressure; CKD: Chronic Kidney Disease; DMSA: Dimercaptosuccinic Acid; Ds-DNA: Double Stranded- DNA; DTPA: Diethylenetriamine Pentaacetic Acid; ESRD: End Stage Renal Disease; LN: Lupus Nephritis; SLE: Systemic Lupus Erythematosus

## INTRODUCTION

Hypertensive emergency is an acute medical condition, characterized by severely elevated blood pressure with end organ damage. Hypertension in children is usually secondary in nature, mostly due to renal diseases. It may manifest as hypertensive emergency or urgency, but most of the time, is detected incidentally. Lupus nephritis is a rare cause, mostly due to the lower prevalence of Systemic Lupus Erythematosus (SLE) in pediatric age group. Although the organ damage caused by hypertension is potentially reversible, it depends on the stage at which the treatment is instituted. Any potential delay in management adversely affects the outcome.

## CASE PRESENTATION

Sixteen-year-old adolescent girl presented with complaints of progressive blurring of vision for one week. It was associated with

frontal headache and intermittent episodes of blackouts. There was no history of decreased urine output/ swelling/ seizures/ focal deficits/ breathing difficulty/ joint pain/ oral ulcers.

On examination, she had pallor, periorbital puffiness and alopecia with high blood pressures (BP) (BP: 182/140 mmHg), BP in all limbs being comparable. There were no focal neurological deficits/ signs of heart failure/bruit over renal arteries; with rest of systemic examination being normal. Fundoscopy revealed Grade IV hypertensive retinopathy (Figure 1 & 2). Investigations revealed normocytic normochromic anemia (Hemoglobin: 7.9g/dL), deranged renal functions [Blood urea: 60 mg/dl; Serum creatinine: 3.7 mg/dl; estimated Glomerular Filtration Rate of 22.4 ml/min/1.73 m<sup>2</sup>] with hypocalcemia (8.1mg/dL) and proteinuria (~100mg/dL). Considering secondary causes for hypertension, further investigations were planned. Renal ultrasound showed

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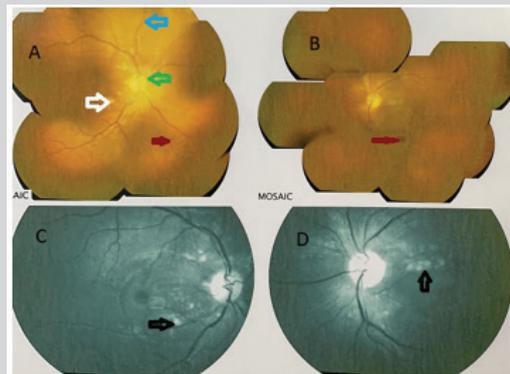
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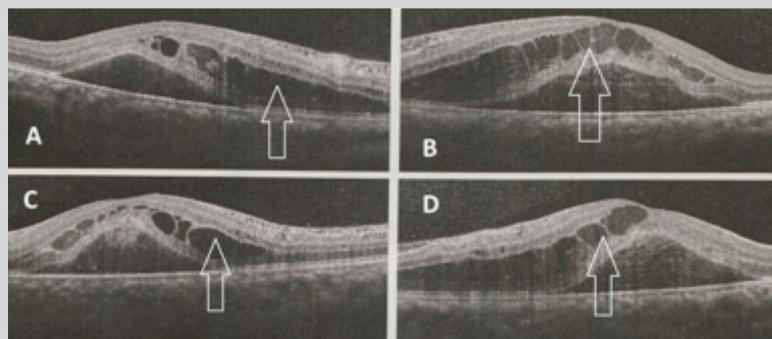
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small kidneys (right: 6.8cm x 2.75cm and left: 7.1cm x 3cm) with raised echogenicity and normal renal doppler, suggestive of chronic kidney disease (CKD). Further workup revealed low Vitamin D levels (72nmol/L) with raised Parathormone levels (1034.8pg/mL) and low Iron (34mcg/dL) and ferritin levels. Tc99m-dimercaptosuccinic acid (DMSA) and Diethylenetriamine pentaacetic acid (DTPA) scan showed globally impaired renal function (GFR: 25.87ml/min- left: 14.49ml/min and right: 11.39ml/min) with no scarring (Figure 3). Structural heart disease was ruled out by echocardiography. Etiological workup of CKD revealed normal C3 and C4 levels with negative anti Streptolysin-O titers and Direct Agglutination Test.

Anti-Nuclear Antibody (ANA) was positive with mitosis positive centrosome and midbody pattern along with positive anti double stranded- DNA (ds-DNA) antibodies. Renal biopsy was suggestive of End Stage Renal Disease (ESRD) showing fibrosis with atrophic tubules (Figure 4-6). Hence, diagnosis of lupus nephritis was made. She was initially stabilized on IV labetalol and Mean Arterial Pressure reduction attained as per protocol. After initial stabilization, enalapril and later on amlodipine were added in view of persistent stage I hypertension. On follow up, visual acuity improved with no residual deficit along with control of BP. She is on renal replacement therapy and doing well on follow up.



**Figure 1:** Fundoscopic image (A- right, B- left) with red free filter (c- right, D- left) showing multiple hemorrhages (red arrow), cotton wool spots (white arrow), perivasculature clearing (blue arrow), hard exudates (black arrow) and optic disc swelling (green arrow), findings suggestive of malignant hypertension.

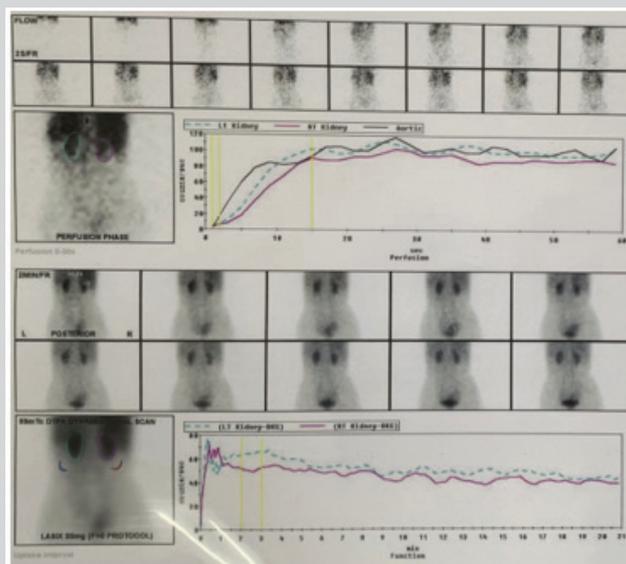


**Figure 2:** Optical coherence tomography showing bilateral cystoid macular edema- (A and C- Right eye; B and D- Left eye): collection of fluid in intraretinal space, due to increased intravascular pressure and fluid exudation- indicating the possibility of central retinal vein occlusion.

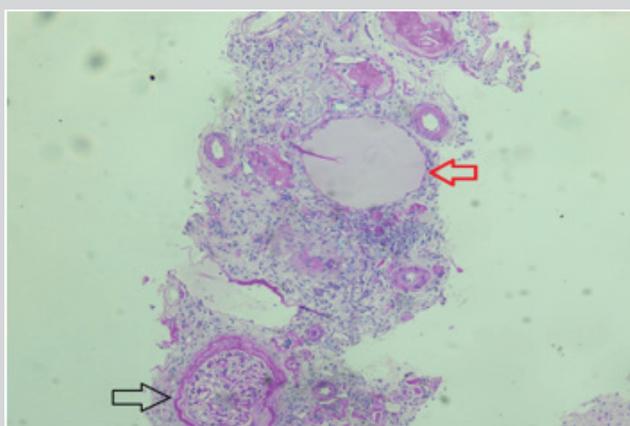
## DISCUSSION

Our index case presented with hypertensive emergency and was later diagnosed with lupus nephritis as the underlying etiology for End Stage Renal Disease. Renal diseases are the most common underlying cause of hypertension in children. Congenital anomalies of Kidney and Urinary tract is the most common etiology in children less than 12 years. Glomerular diseases are more common in children above 12 years of age [1]. Most of the cases are incidentally detected. It may also present as hypertensive urgency and emergency, manifesting as headache, visual changes, nausea, seizures, dizziness or epistaxis. It is characterized pathologically by increased intima-media thickness of arteries, left ventricle hypertrophy, increased arterial stiffness and glomerular and retinal changes [2]. Secondary hypertension has more propensity of developing into hypertensive crisis. Since most of the cases are

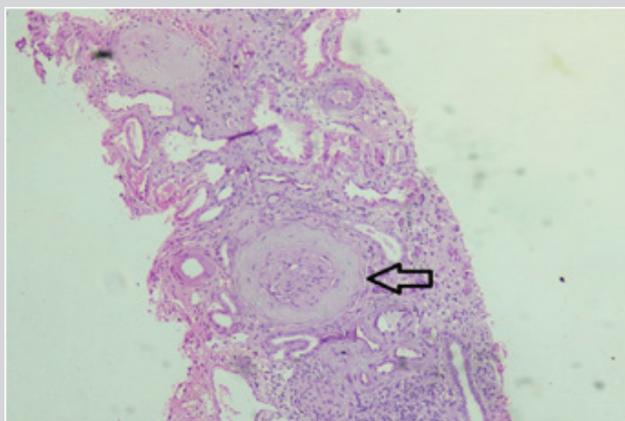
asymptomatic and the prognosis is better when the disease is diagnosed early, it is prudent that all children above the age of three years should undergo an annual BP measurement [3]. Secondary hypertension evaluation is guided by the etiology specific to that particular age group and sex, like- renal parenchymal disease, endocrine causes, coarctation of aorta and essential hypertension. Careful clinical history is followed by baseline investigations including complete blood count, renal function tests and urine examination for proteinuria and hematuria (for glomerular involvement). Specific tests include vitamin D levels, parathormone and iron studies (chronic kidney disease), C3/C4 complements, Direct Agglutination Test, ANA and anti-dsDNA antibody titres for SLE, Anti-Nuclear Cytoplasmic Antibody (ANCA) for vasculitis, renal ultrasound-doppler to look for renal artery stenosis, and hormonal studies (endocrine causes). DMSA and DTPA scan are done for structural and functional assessment of kidneys.



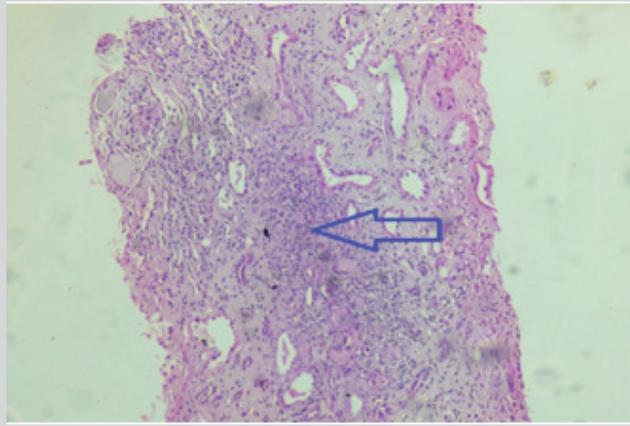
**Figure 3:** Diethylenetriamine pentaacetic acid (DTPA) scan showing decreased contrast clearance from both kidneys- plateauing of tracer levels in bilateral renal parenchyma and aorta- suggesting decreased Glomerular Filtration Rate.



**Figure 4:** Photomicrograph (Hematoxylin and Eosin- 100X magnification) of renal biopsy specimen showing tubule with squamous epithelium (red arrow) and intraluminal colloid deposition- suggestive of thyroidisation. Normal glomerulus marked in black arrow.



**Figure 5:** Photomicrograph of renal biopsy specimen (Hematoxylin and Eosin- 100X magnification) showing sclerosed glomerulus with periglomerular fibrosis. Most of the glomeruli examined in other fields were also sclerosed, suggestive of End Stage Renal Disease.



**Figure 6:** Photomicrograph of renal biopsy specimen (Hematoxylin and Eosin- 100X magnification) showing inflammatory cells' infiltration- predominantly lymphocytes with fibrosis in interstitium- suggestive of chronic inflammation.

Assessment for target organ damage includes an Electrocardiogram and Echocardiography to evaluate for left ventricular hypertrophy (LVH); and fundoscopy for hypertensive retinopathy [4]. LVH can occur in around 34% to 38% of the cases and mandates the intensification of therapy. Presence of retinopathy can be considered as a non- invasive marker of nephropathy [5]. Negative correlation between glomerular filtration rate (GFR) and retinopathy stage was also evident in our case.

Lupus nephritis is a rare cause of hypertensive emergency in children and is more severe than its adult counterpart [6]. Although it occurs in around 37-82% of children affected with SLE, the overall contribution is low due to less prevalence of SLE itself, the incidence of the same being 0.36-0.9/100,000 children/year [7]. To prevent rapidly evolving end-organ damage, patients with hypertensive emergency need prompt institution of BP reduction. IV labetalol is the most common first line therapy due to its efficacy and safety in children. Mean Arterial Pressure reduction should not exceed more than 25% over the first eight hours with complete normalization over next 24-48 hours. Rapid blood pressure reduction may lead to visual defects, renal insufficiency and permanent neurological sequelae.

Treatment of lupus nephritis (LN) consists of two phases: induction phase (three to six months) and maintenance phase (uptil three years). It predominantly depends on the stage of LN. Mycophenolate Mofetil (MMF) or cyclophosphamide is used for induction therapy. Hydroxychloroquine can also be used in such cases due to its potential benefit of reducing the renal damage. Immuno- globulin, plasma exchange or Rituximab may be used in refractory cases. Azathioprine, MMF or prednisolone may be used for maintenance therapy. Exacerbations are treated akin to first episode and in spite of early treatment, there is 10-20% chances

for progression to ESRD. But if the diagnosis is delayed and lupus nephritis has progressed to ESRD as in our case, homeostasis cannot be maintained by medical therapy and may mandate hemodialysis or renal transplantation- the ultimate goal being the renal transplant for these patients after achieving immunological remission.

The presenting case reiterates the need for prompt evaluation and treatment in hypertensive emergency which is the key to prevent the irreversible damage in such cases. Considering multisystemic disease like SLE as the potential underlying etiology is of paramount importance which is often neglected in such cases with atypical presentation.

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