Case Report

A Case of Membrano-Proliferative Glomerulonephritis with Posterior Reversible Encephalopathy Syndrome (PRES)

Rafia Jamil[1], Bushra Ahmad[2], Sarah Iqbal[3], Farnaz Abbas[4], Mahjabeen Masood[5], Muhammad Haroon Hamid[6]

[1,2,6]Pediatric Medicine Unit 1, KEMU/ Mayo Hospital, Lahore; [3]Histopathology Department, Mayo Hospital, Lahore; [4,5]Department of Radiology, KEMU/ Mayo Hospital, Lahore

Abstract

Membranoproliferative glomerulonephritis (MPGN) is an uncommon variety of nephrotic syndrome in children which is often associated with hypertension. Posterior reversible encephalopathy syndrome (PRES) is a rare and serious outcome of severe hypertension characterized by acute onset of headache confusion and seizures along with radiological findings. This syndrome has been described rarely in children. We report here a case of a 10-year-old girl with steroid resistant nephrotic syndrome, later proved to be MPGN on renal biopsy that developed PRES due to persistent severe hypertension. She recovered with appropriate treatment.

Corresponding Author | **Dr. Rafia Jamil,** Pediatric Medicine Unit 1, KEMU/ Mayo Hospital, Lahore. **Email:** rafiajamil15@gmail.com

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Introduction

Nephrotic syndrome is a constellation of glomerular diseases associated with heavy proteinuria (more than 3.5g/24hour), hypoalbuminemia, edema and hyperlipidemia. The annual incidence of nephrotic syndrome is 2-7 cases per 100,000 and the prevalence is around 16 cases per 100,000 children.[1] Almost 90% cases of nephrotic syndrome are idiopathic and about 7% of these cases are due to membranoproliferative glomerulonephritis. It occurs in young adults and children with no gender predilection. These patients often have a variable clinical course and a mixed nephritic-nephrotic clinical picture.[2] Hypertension is present in approximately one-third of the patients which is typically mild and rarely leads to any serious outcome. Severe hypertension, if present, may lead to posterior reversible encephalopathy syndrome (PRES), which is a serious clinicoradiological condition characterized by acute onset headache, altered sensorium, visual changes, seizures and white matter vasogenic edema affecting posterior occipital and parietal lobes of the brain as seen on MRI.[3] It is, however, mainly described in adults and uncommonly in children.

Case Report:

A 10-year-old girl presented to Mayo Hospital with generalized body swelling involving face, abdomen and feet with no history of rash, joint pains, hematuria or family history of autoimmune diseases. On examination, she had blood pressure of 130/80 mmHg (above 95th percentile for age), periorbital puffiness, pedal edema of grade 4, massive abdominal distension and decreased air entry at lung bases. Laboratory investigations revealed hypoalbuminemia (2g/dL). Urine analysis showed proteinuria (3+) and microscopic hematuria (20-30/HPF), spot urine protein creatinine ratio was (9.8). Her renal function

tests were normal. Lupus serology including ANA, anti ds DNA levels and complement levels were also normal. Screening for HIV, hepatitis B and C was performed which was negative. Abdominal ultrasonography showed mild pleural effusion and abdominopelvic ascites. With clinical diagnosis of atypical nephrotic syndrome, treatment was started with prednisolone (60mg/m^2/day) and an antihypertensive drug along with supportive care.

Despite 4 weeks of steroid therapy, her generalized edema and proteinuria did not improve. Considering steroid resistant pattern, renal biopsy was done and immunosuppressant drug tacrolimus was started. Renal biopsy specimen showed membranoproliferative glomerulonephritis (MPGN) type I histology, on the basis of diffuse membranoproliferative/ endocapillary proliferation pattern of glomerulonephritis. Sclerosis and crescent formation were not seen. Immunofluorescence staining demonstrated deposits of IgG and C3 in the mesangial region and capillary wall.

During treatment, the patient developed sudden headache, dizziness, altered sensorium and generalized tonic clonic fits followed by post ictal drowsiness. She had blood pressure of 170/110 mmHg at that time. Neurological examination showed normal tone, power and deep tendon reflexes bilaterally. Cranial nerve examination was normal. CT brain plain showed a triangular hypodense area in right frontal lobe and small hypodense regions in both parietal lobes, involving both gray and white matter suggestive of infarct or ischemic changes.

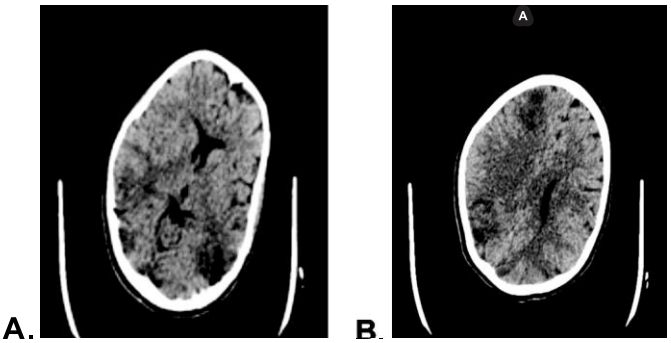

Figure 1: *Plain computed tomography scan showing; (A) symmetrical hypodensities in bilateral parietal cortex at the level of third ventricle suggestive of posterior reversible encephalopathy syndrome. (B) A patchy hypodense area with loss of grey-white matter differentiation is seen in right frontal region at the level of lateral ventricles.*

The patient was then treated by a combination of multiple antihypertensives including furosemide, ramipril and diltiazam and an anti-seizure medication, phenytoin. Her sensorium improved with supportive care and above treatment, and she did not have any further seizures. An MRI was done later on, which showed that initial cerebral lesions evident on CT scan had resolved completely.

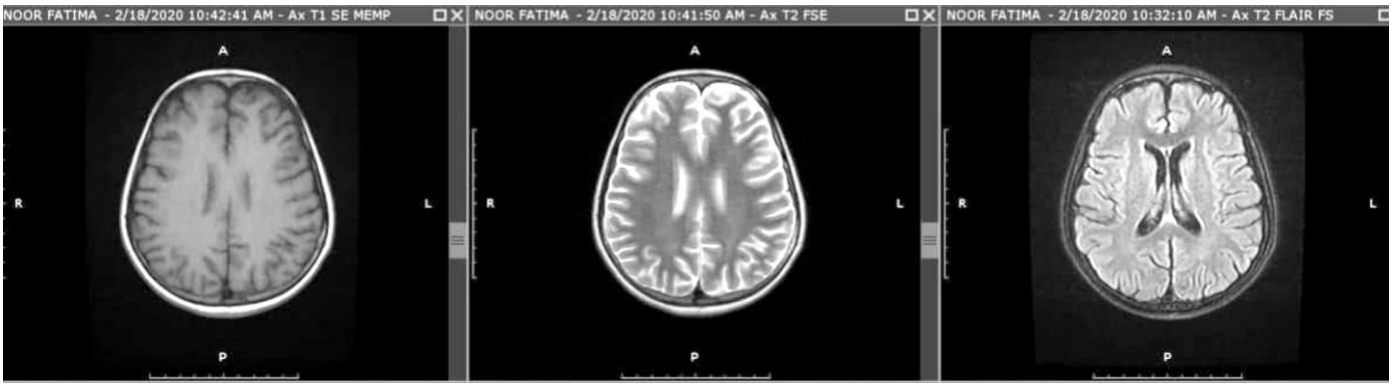

Figure 2: *Axial MRI images at the level of third ventricle showing no abnormality.*

Discussion:

Patients with nephrotic syndrome may sometimes present with atypical features like gross hematuria, hypertension, hypocomplementemia and azotemia that necessitates the need for a renal biopsy. As seen in our case, along with typical features of nephrotic syndrome, patient had hypertension and microscopic hematuria and was unresponsive to steroid therapy. Therefore renal biopsy was done that showed histological pattern of membranoproliferative glomerulonephritis. MPGN can be idiopathic or secondary to autoimmune diseases, infections (hepatitis B & C,

syphilis) or carcinomas. It shows a variable clinical picture termed as nephriticnephrotic phenotype. About 80% of the cases have hypertension at presentation.[4] More than 50% have azotemia and they are likely to have low serum complement levels.[5] Our patient presented with idiopathic MPGN associated with hypertension, although azotemia and hypocomplementenemia were absent. Due to its rarity, the definitive treatment of idiopathic MPGN is not yet clearly defined; various therapeutic treatment regimens have been tried but due to small number of patients controlled trials are not available.[6] Corticosteroid therapy is primarily given to all the cases of membranoproliferative nephrotic syndrome[7], as we did in our case. However, when our patient did not go into remission after 4 weeks of steroid therapy, we started an immunosuppressant; tacrolimus- a calcineurin inhibitor. Our choice was based on previous studies where Hadad et al[8] treated two cases of MPGN and Butani et al[9] treated a few cases of steroid resistant nephrotic syndrome successfully with tacrolimus. Our patient too, fortuneately responded to tacrolimus. The prognosis of MPGN is uncertain. Only a small number of patients undergo remission and the presence of hypertension, nephrotic syndrome and renal insufficiency are known poor prognostic factors. Unfortunately, hypertension and nephrotic-range proteinuria were present in our patient but she has shown a good response to tacrolimus.

An important event that occurred during treatment was the development of posterior reversible encephalopathy syndrome (PRES). It was first reported by Hinchey et al in 1996[10] and was defined as a reversible, posterior leukoencephalopathy in patients who have hypertension, renal impairment or those who are on immunosuppressive therapy. In our case, risk factor was the presence of persistent hypertension. PRES was initially thought to be rare in childhood but studies conducted in recent past reported its increased prevalence in children.[11] Symptoms include severe headaches, nausea, lethargy, seizures, stupor, coma and/or visual disturbances along with the neuroimaging abnormalities characterized by partially or completely reversible vasogenic edema in the posterior white matter.[12] MRI is the preferred diagnostic modality. However, alterations suggestive of cerebral edema are also visible on CT scan.[13] Our patient developed severe headache, confusion and fits. No visual disturbance was reported. Her CT scan showed hypodense areas in frontal and parietal zones that are specific changes for PRES. These lesions, however, resolved completely as suggested by follow-up MRI. In these cases, the symptoms and radiological findings resolve within a few hours to few weeks. However, a delay in diagnosis and treatment may lead to irreversible neurological deficit. Hence, if a child with nephrotic syndrome presents with seizures or coma, PRES should also be considered as a differential diagnosis. A lower threshold for diagnosis and immediate control of blood pressure, anti-convulsive therapy and discontinueation of the causative agent results in best outcome of PRES, as happened in our case.

Suggested by previous studies, calcineurin inhibitors are also notorious for precipitating PRES [11, 14]. And as our patient could not get remission of nephrotic syndrome with steroids, tacrolimus was started. However, her blood pressure was strictly kept within normal limits and fortunately, no other episode of PRES occurred after starting tacrolimus and eventually our patient got into remission of not only PRES but also nephrotic syndrome.

Ethical Approval: Given
Conflict of Interest: The authors declare no conflict of interest
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