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Malignant hypertension as the initial symptoms in a patient with mesangioproliferative glomerulonephritis: a case report and review the literature

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Abstract: **Some patients, especially the type 2 MPGN could have malignant hypertension, but type 1 MPGN patient who have Malignant hypertension were seldom reported. A 16-year-old man was admitted to our hospital with a known history of hypopsia for abnormal vision loss and decrease in renal function. Renal pathology hint of primary membrane proliferative glomerulonephritis. The clinical manifestations of patients with malignant hypertension and renal insufficiency. Patients with clinical symptoms were significantly relieved when given anti-infective, antihypertensive therapy. Kidney Essential Hypertension is the most common secondary hypertension, accounting for the second most common cause of hypertension in adults. To the first manifestations of malignant hypertension as the primary MPGN is rare, in the course of treatment should be based on the control of blood pressure on the active treatment of primary disease.**

Keywords: Malignant hypertension; MPGN; C3

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1. Introduction

Membranous proliferative glomerulonephritis (proliferative glomerulonephritis, MPGN) is one of the uncommon clinical refractory glomerulonephritis, also known as mesangial capillary glomerulonephritis, which is characterized by Glomerular basement membrane thickening, mesangial cell proliferation and mesangial stromal expansion. Clinically, this group of patients with disease often manifested as nephrotic syndrome with hematuria, hypertension and renal dysfunction. Some patients with persistent hypotension, it is also known as hypotension chronic nephritis. Pathological types of MPGN can be divided into primary and secondary, secondary MPGN common causes include infection, autoimmune diseases, abnormal proteinemia, chronic hepatitis and diabetic nephropathy. Primary membranous proliferative glomerulonephritis is divided into three types according to pathological manifestations. The diagnosis of the disease based on the main reference to pathological examination. Once the renal pathological diagnosis of MPGN, should be carefully looking for secondary factors, especially for those in middle-aged patients. Because it is critical for the patient to determine the treatment and prognosis. MPGN can occur at any age, acute nephritis syndrome and nephrotic syndrome is one of the most classic clinical phenotypes. 50 ~70% of the patients with persistent serum C3 down to mesangial cell proliferation and mesangial matrix expansion, basement membrane thickening of [1]. Light visible mesangial cells and matrix hyperplasia, insert the glomerular basement membrane (GBM) and endothelial cells, PASM staining GBM is "dual-track", see mesangial area and Masson staining in subcutaneous get addicted to the complex red protein deposition, most advanced capillary atrophy or occlusion, beads were lobulated. Renal pathological examination should pay attention to moderate and severe mesangial proliferative glomerulonephritis phase identification. Malignant hypertension as the initial symptoms in a patient with mesangioproliferative glomerulonephritis is rare. In this paper, the malignant hypertension as the initial symptoms in a patient with mesangioproliferative glomerulonephritis report.

2. Case presentation

A 16-year-old man was admitted to our hospital on December 7, 2014, with a known history of hypopsia for over 1 week, fever, cough and tiredness for 1 day. 1 week before admission, the patient present progressive vision loss without notable predisposing factors and he did not receive any treatment. 1 day ago, patients developed fatigue associated with cough, sputum, fever which was up to 39℃. Blood pressure was 160/ 190 mmHg. Blood routine examinations showed that white blood cell, 10.06×10^9/L; Neutrophil, 85.9%; Hemoglobin, 110g/l; CRP, 3.3mg/l. Emergency Blood chemistry findings included potassium, 5.2mmol/l; calcium, 1.53mmol/l; urea nitrogen, 9.4mmol/l; creatinine, 171umol/l. Emergency department diagnosed the patient as renal insufficiency, then nephrology department admitted him. Patient was healthy before, and his parents were both healthy and denied any family history.

Physical tests after admission were as follows.

Temperature, 38.4℃; Pulse, 106/min; Blood pressure, 211/126mmHg. The patient had clear consciousness and coarse breath sounds without rhonchus and moist rales. Heart rate was 95/min with a normal heart rhythm, and carried no pathologic heart murmurs. Abdomen was soft, no tenderness or rebound tenderness. There was no kowtow painful in kidney area, and no edema of lower extremity. Admission diagnosis were as follows: 1.Renal insufficiency; 2.Malignant hypertension; 3.Respiratory tract infection.

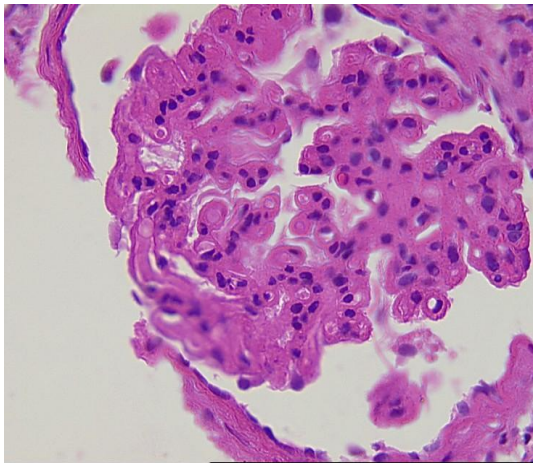

Figure 1. HE×400.

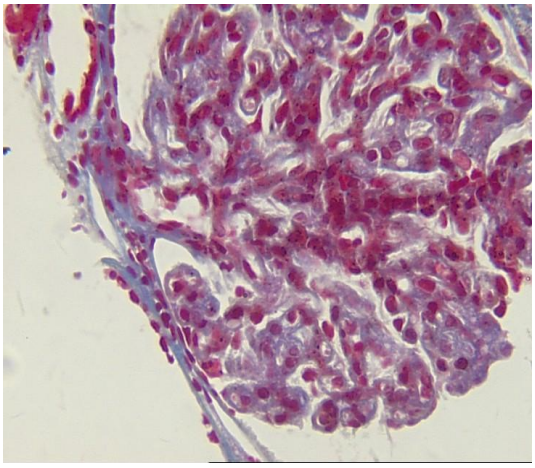

Figure 2. Masoon×400.

Analysis of urine after admission was shown that occult blood ++, urine protein +++, urine specific gravity 1.006; the red blood cell shape and counting in urine was 10000/mL, malformed red blood cells was 90% and bacillus was 5%; total quantity of urinary protein 3.10g/24h; blood routine examination indicated that hemoglobin 107g/L, leucocyte count 10.98×10^9/L,percentage of neutrophils 86.6%; biochemical assay revealed that albumin 21.96g/L, urea 9.59mmol/L, creatinine 183umol/L, total cholesterol 8.86mmol/L, triglyceride 4.42mmol/L, erythrocyte sedimentation rate (ESR) 25mm/h, c-reactive protein (CRP) 13.40mg/l; Humoral immune function assays suggest that immunoglobulin G 2.48g/L, complement C30.455g/l, Parathyroid hormone 102.0pg/ml; Bacteriological examination of sputum showed that WBC >25/LP , normal flora without fungi, TORCH IgM were both negative; Concentration of urinary vanillylmandelic acid (VMA), Cortisol rhythm, blood transfusion examination, 9 tests on respiratory pathogens, anti glomerular basement membrane antibodies, auto antibody test, ANCA and subtypes, tumor associated material examination, calcitonin angiotensinogen, detection of the 5 serological markers of Hepatitis B, 4 index signs of coagulation bloods, stool routine detection showed no obvious abnormity. Double renal artery and vein color doppler ultrasonography was normal; color doppler ultrasound on urinary system suggest that there were enhancing echolocations in renal parenchyma from both sides; color doppler ultrasonography on hepatobiliary tract, pancreas and spleen had no obvious abnormity or seroperitoneum; color doppler ultrasound on cardiac detected that ventricular septum and posterior left ventricular wall had hypertrophy; chest CT scan showed that there was a fiber lesion on the upper lobe of the right lung which was considered that the lower lobe of the left lung had inflammation, and there were a few atelectasis tissues on the lower lobe of the right lung, and pleural effusion happened on both sides; unenhanced CT of adrenal had no abnormity.

Diagnosis and treatment: ophthalmic consultation after admission, physical examination showed that the vision of the right eye was 1mile before eyes and corneal was transparent in both eyes. Pupils were orbicular and the diameter of them were about 4mm and the pupilary light reflex was sensitive. Ocular fundus examination showed papilloedema, tortuous veins and thinning arteries; the posterior pole of retinal was edema in which there were large amounts of cotton-wool spots; the region of macula was edema and reflection of it was not clear. The vision of the right eye was 10 mile before eyes which had papilloedema, tortuous veins and thinning arteries too. And in the posterior pole of retinal, retinal edema, patchy hemorrhages, and numerous cotton-wool spots could be seen. Additionally, macula area was edema, and there were hemorrhages and cotton-wool spots. Diagnosis: hypertensive retinopathy with fundus hemorrhage. After hospitalization, patient received combined treatment of Adalat GITS, Amlodipine and Olmesartan to control blood pressure and keep it between 150~180 or 80~100mmHg. Piperacillin-tazobactam and Reduning were used to anti-infective for 3days, and after that symptoms of fever, cough and expectoration were improved. Daily urine volume of patient fluctuated from 1500 to 3000mL. 2014-12-10 To suppress the immune system so that Prednisone (40mg/day, intravenous instillation) was given to the patient. 2014-12-11 Renal function examination showed that urea 13.01 mmol/L, creatinine 276umol/L. Under the guidance of B-mode

ultrasound, patient received kidney puncture and returned to the ward safely.12-21 Renal function examination showed that urea 16.07mmol/L, creatinine 156umol/L, blood pressure still fluctuated between 150~170/80~100mmHg. The patient left hospital with a better health condition. Discharge diagnosis:1. membranoprolifer ative glomerulonephritis 2.malignant hypertension severe hypertensive retinopathy 3. Pneumonia.

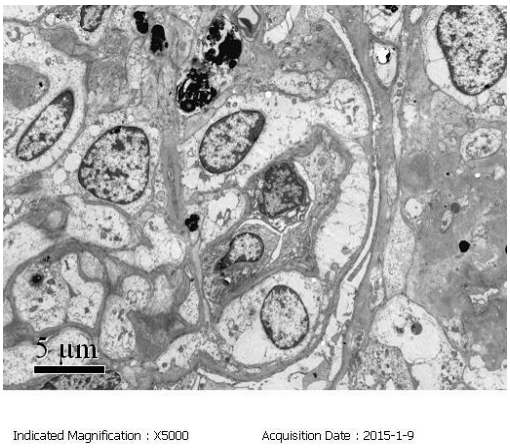

Figure 3. Electron microscope.

Renal biopsy and pathological: light microscope: 2 regions of medullary renal tissue. Two glomerular sclerosis of 12 glomerular and the last were lobulated, and there were mild-to-moderate hyperplasia and segmental insertions in glomeruli mesangial cells and matrix; capillary loops were stiffer and poor opening with capsular synechia and segmental thickening (Figure 1). PASM－Masson showed that basement membrane had segmental thicknening without obvious red complex deposition. There were almost 40% atrophy of renal tubular, and the rest tubular epithelial cells were swelling and granular degeneration in which we could see a little protein casts, renal interstitial edema, fibrosis(++), many clusters of foam cells and inflammatory cell infiltrated, the wall of small interstitial arteries thickening and partial glass-like degeneration(Figure 2). Immunofluorescence showed that 5G, IgG-, IgA-, IgM++, C1q-, C3++, FIB-, K-, λ-, HBsAg-, HBcAg-,which were granular deposited in the segmental mesangiaregion area. Electron microscope (The first people's Hospital of Peking University) described that there were moderate-to-severe hyperplasia and widely insertions in glomeruli mesangial cells and matrix, and the loose layer of basement membrane were segmental broadened combined with tram line sign without obvious electron dense deposits, and epithelial cell foot processes segmental fused. There were vacuolar degeneration and increased lysosomes in renal tubular epithelial cells. No obvious pathological changes were found in renal interstitial. Pathologic diagnosis: Membranoproliferative glomerulonephritis (Figure3-4).

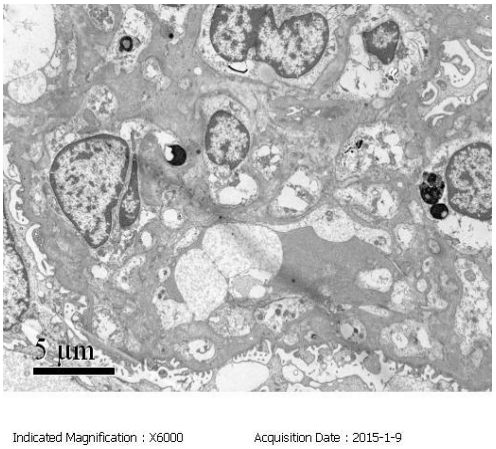

Figure 4. Electron microscope.

In the comprehensive consideration of the patient's age, fertility requirements, economic conditions and other factors, we still use Medrol 16mg/day and use an extra dose of Leflunomide 20mg/day to suppress immunity [1]. The dose of hormone was reduced gradually. After treatment for 3 month, proteinuria became negative and 24 hours proteinuria was 0.3g.Then we gradually decrease the dosage of Medrol and Leflunomide, and stopped use them after treatment for half a year. Now the patient only takes blood pressure drugs.

3. Discussion

Membranoproliferative glomerulonephritis (MPGN) is an intractable glomerular nephritis which is rare in clinic and characterized as mesangial cell proliferation, mesangial matrix expansion and basement membrane thickening [2]. MPGN can occur at any age, acute nephritis syndrome and nephrotic syndrome is the most classic clinical manifestations. 50% to 70% of patients with persistent serum C3 decreased. According to etiology, MPGN can be divided into primary and secondary type [3]. We define primary MPGN as no secondary factors after further examinations of chronic infection, immunology and pathology. Further, primary MPGN could be divided into 3 types according to their pathological characteristics. Optical microscopy of this patient showed that glomerulosclerosis was lobulated; mesangial cell and matrix were diffuse proliferative and segmental inserted. And Immunofluorescence showed that IgM and C3 were located in mesangial areas which and in the form of granules [4]. Electron microscope found that there were moderate-to-severe hyperplasia and widely insertions in glomeruli mesangial cells and matrix but no clear electron dense deposits accumulation was detected, which accorded with type 1 membranous proliferative glomerulonephritis.

The patient in this case was a young male. His blood pressure raised rapidly and seriously that diastolic

pressure was up to 130mmHg. Simultaneously, it accompanied by fundus hemorrhage and exudation which met the diagnosis of malignant hypertension [5]. Usually, hypertension was mild which happened in membranous proliferative glomerulonephritis. Some patients, especially the type 2 MPGN could have severe hypertension, but type 1 MPGN patient who have malignant hypertension were seldom reported [6].

Proteinuria analysis showed that urine protein quantity of the patient was 3.10g/24h which did not decreased with the control of blood pressure, while creatinine increased progressively. Ultrasound observation on both sides of renal showed that the patient had normal renal size, but echoes of parenchyma were enhanced which was considered with chronic kidney damage. The patient had acute onset for malignant hypertension combined with kidney injury. This case was given to the possibility of IgA glomerulonephritis complicated with malignant hypertension, but we could not exclude crescentic glomerulonephritis. As a result, methylprednisolone (40mg/ day, intravenous instillation) was used to suppresses inflammation, resuce interstitial edema and improve renal function after we controlled infection and blood pressure. Renal biopsy of the patient showed that MPGN, and no typical characteristics of renal damage in primary malignant hypertension such as fibrinoid necrosis of afferent arteriole, onion skinning necrosis of intimal and thrombosis under microscope. And series of examinations includes cortisol biorhythm, urine VMA and adrenal CT did not find obvious abnormality. This confirmed malignant hypertension of the patient was caused by primary MPGN. 2011 KDIGO published guidelines for the treatment of glomerular diseases recommended for clinical manifestations of renal function in patients with MPGN, given hormone combined with cyclophosphamide or mycophenolate mofeti [7]. At present, there is no unified program for the treatment of MPGN. Most of the literature think that the preferred treatment for MPGN is Glucocorticoid, Many scholars adhere insist the long-term high-dose hormone maintenance therapy as the main treatment of MPGN treatment [8,9]. Although KDIGO introduced the use of a small dose of hormone combined with oral cyclophosphamide or mycophenolate mofetil, these observations were derived from a small sample data without evidence of RCTs research [7].

Poor prognosis of MPGN patients is related to renal pathological type, type 1 MPGN better than type 2 prognosis. Factors associated with type 1 MPGN prognosis include hypertension, impaired renal function, nephrotic syndrome, and crescent formation.

This case is a primary MPGN in which initial clinical manifestation is malignant hypertension, and it is rare in clinic. So we should treat the primary disease actively on the basis of controlling blood pressure during the process of treatment.

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