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ПРИКАЗ БОЛЕСНИКА / CASE REPORT
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Oligomeganephronia: Case Report and Literature Review

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SUMMARY
Introduction Oligomeganephronia (OMN) is one of rare congenital kidney disease. The number of nephrons reduces and the volume of glomerulus increases. The incidence of OMN is uncertain because it is difficult to diagnose. There are no any special clinical manifestations of OMN. Renal pathology is the only way to diagnose OMN, so missed diagnosis always happens without renal pathology.
Case Outline A 26-year-old male was diagnosed OMN associated with proteinuria and increased serum creatinine. The size of both kidneys on ultrasound was smaller than normal. Pathological features involved a reduced number of greatly enlarged glomeruli indicating OMN.
Conclusion OMN is a rare disease and it has been rarely reported. The exact mechanism is not clear. The diagnosis mainly depends on pathological findings. For patients with OMN, proteinuria and renal dysfunction are often the main cause to visit a doctor. Early diagnosis is important.
Keywords: oligomeganephronia; renal pathology; diagnosis

INTRODUCTION

Oligomeganephronia (OMN) is a rare congenital renal hypoplasia [1, 2] featuring a reduced number of nephrons and increased glomerular volume. For patients with OMN, proteinuria and renal dysfunction are often the main cause to visit a doctor. The final outcome of patients with OMN is inevitably the end stage renal disease (ESRD). The incidence of OMN is uncertain because it is difficult to diagnose. There are no any special clinical manifestations in patients with OMN. Renal pathology is the only way to diagnose OMN, so missed diagnosis always happens without renal pathology.

We report an episode of OMN associated with proteinuria and increased serum creatinine. The size of both kidneys on ultrasound was smaller than normal. The pathological features were diagnosed based on the reduced number of greatly enlarged glomeruli indicating OMN. We also discuss the topic as reported in the medical literature.

CASE REPORT

A 26-year-old male was admitted to Qilu Hospital with proteinuria and increased serum creatinine. He had a history of proteinuria lasting for two years and increased serum creatinine lasting for ten days. He did not have a history of hypertension, diabetes mellitus, systemic lupus erythematosus, hepatitis and tuberculosis.

At the time of admission, his blood pressure (BP), heart rate and temperature were normal. His examination did not reveal any petechiae, ecchymoses or peripheral edema. On admission, blood urine nitrogen (BUN) was 11.15 mmol/L, serum creatinine (SCr) 160 μmol/L, and creatinine clearance rate (Ccr) 62.11 ml/min. Microalbumin, IgG, and β2-microglobulin (β_2MU) in urine was 242 mg/L, 24.6 mg/L (0-14) and 3.90 mg/L (0-0.22), respectively.

Anti-streptococcal antibodies, anti-glomerular basement membranous antibodies, anti-double stranded DNA antibodies, anti-nuclear antibodies, anti-Sm antibodies, anti-SSA antibodies, anti-SSB antibodies, anti-Scl-70 antibodies, anti-PM-SCL antibodies, anti-Jo-1 antibodies and anti-CEN-P antibodies were all normal. At the same time, the prothrombin time, alanine aminotransferase, aspartate aminotransferase, lactate dehydrogensase, immunoglobulin G, immunoglobulin A, immuglobulin M, completement 3 and completement 4 were also within the normal range. Perinuclear and anti-neutrophil cytoplasmic antibodies (P-ANCA and C-ANCA) were normal as well.

The size of both kidneys was smaller than normal (left 9.7×3.8 cm, right 9.0×3.1 cm). The cortex and medulla of both kidneys on ultrasound were not clear. There was no any caliectasis and pyelectasis in both kidneys and obvious dilatation in the bilateral ureters. The electrocardiogram was normal.

After admission, the patient immediately underwent kidney biopsy using a Super Core biopsy instrument (16ga×15 cm, Medical Device Technologies, INC). We obtained two biopsy specimens, and each specimen about 1 cm long contained 100% cortex with 6 glomeruli. On light microscopy (Figures 1 and 2), the mean diameter of the glomerulus was about 305 μm, which was approximately 1.5 times larger than normal, and the mean glomerular

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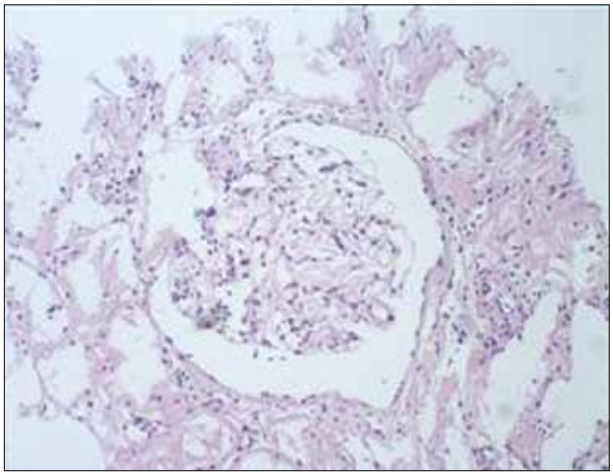

Figure 1. Hematoxylin-eosin staining of glomerulus (×200)

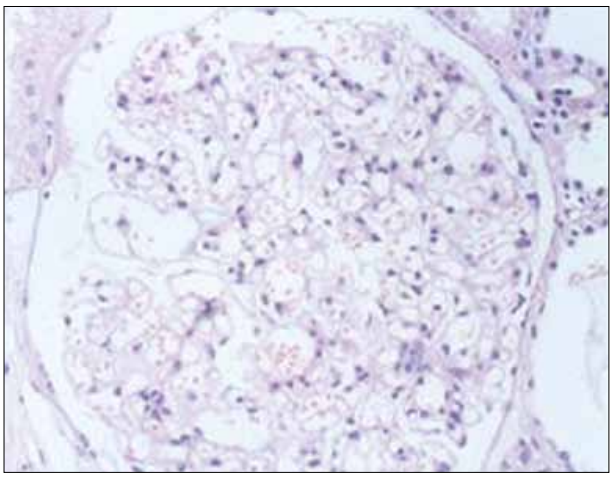

Figure 2. Hematoxylin-eosin staining of glomerulus (×400)

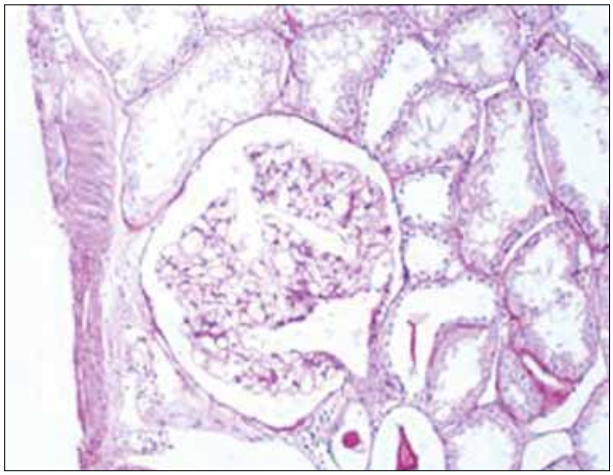

Figure 3. Periodic acid-Schiff staining of glomerulus (×200)

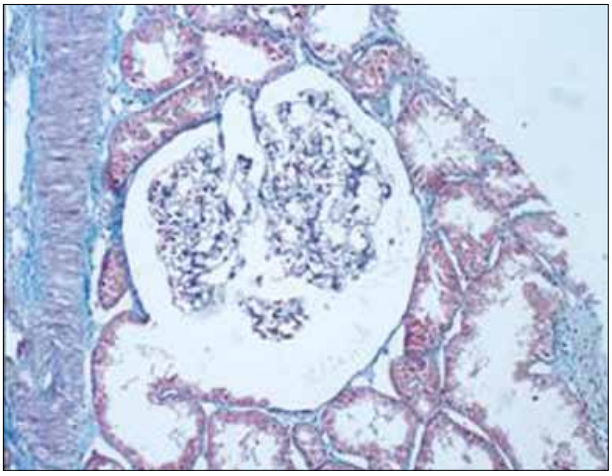

Figure 4. Masson staining of glomerulus (×200)

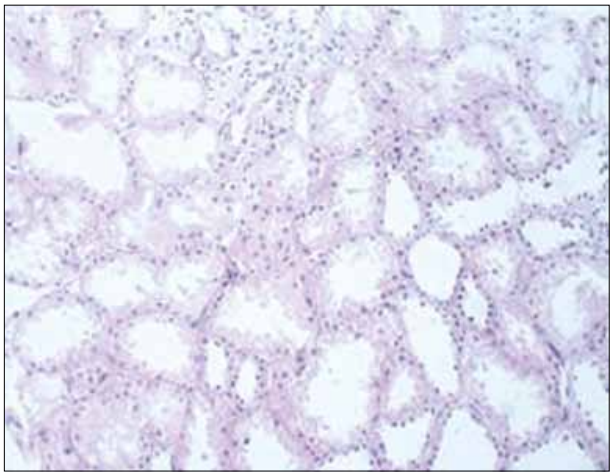

Figure 5. Hematoxylin-eosin staining of glomerulus (×200)

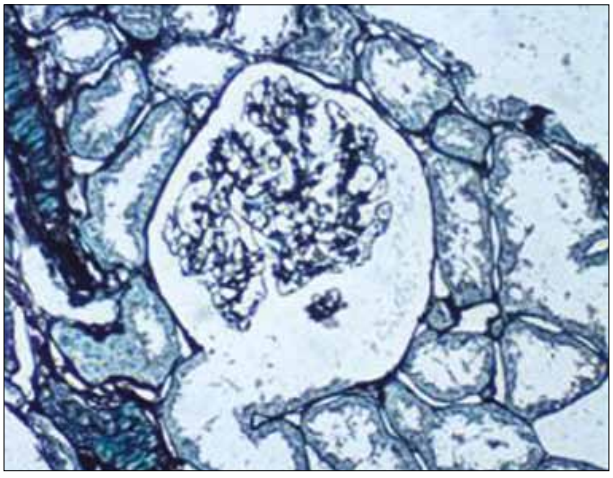

Figure 6. Methenamine silver staining of glomerulus (×200)

volume was about 3.37 times larger than normal. There was no increase in the mesangial matrix of normal morphology. Immunofluorescence of IgA, IgG, C3, fibrinogen, IgM and C1q were all negative. There was no increase in the glomerular capillary wall thickness by Periodic Acid-Schiff (PAS) staining (Figure 3), and no significant complex red protein deposition in the kidney biopsy specimen as determined by Masson staining (Figure 4).

The kidney specimen did not show any tubular injury and had normal tubular epithelial cells. There were no casts in the renal tubular lumen. Interstitial small arteries were all normal. However, the kidney specimen featured interstitial edema, small focal fibrosis and inflammation (Figure 5). Methenamine silver staining is shown in Figure 6.

The diagnosis of OMN was established according to clinical manifestations, imaging findings and renal pathological

features. The patient's OMN was immediately treated with supportive and other therapeutic measures. After ten days, the patient was discharged with decreased serum creatinine and proteinuria than that disclosed on admission.

DISCUSSION

OMN was first reported in 1962 by Royer et al. [3] and Habib et al. [4], as a congenital disease characterized by renal hypoplasia. OMN is a congenital anomaly of bilateral renal hypoplasia, histopathologically featuring a reduction in the number of nephrons and markedly enlarged glomeruli, so the final diagnosis of OMN is based on renal pathologic findings. OMN is one of the reasons that lead to ESRD and so far is rarely reported worldwide [5]. The mechanism of OMN can be either associated with patients' hereditary characteristics, or associated with the nuclear transcription factor PAX2 [6] or the gene mutation of cell transcription factor TCF2 [7]. Perhaps, OMN is one of some clinical manifestations of a certain kind of particular disease [8]. Currently, there is no effective treatment and preventive measures for OMN because of unclear mechanism. Regular follow-up is needed.

Patients with OMN are often born with a lower birth weight than a normal newborn. In the neonatal period, it can appear with one or more of the following abnormalities: pneumothorax, feeding difficulties, metabolic poisoning and excessive urinary sodium, etc. More than fifty percent of children with OMN experience weak constitution in babyhood. Children with OMN aged below one year can also have growth retardation unrelated to kidney function [9, 10]. A vast majority of patients with OMN show first clinical manifestations before the age of 20, accounting for 62.5% [11]. Our patient was born with BW of 3.0 kg, which is within the normal range, and there were no any abovementioned symptoms during his neonatal and infancy periods. The ages when proteinuria and elevated serum creatinine are diagnosed for the first time are 24 years and 26 years, respectively.

The common clinical manifestation in patients with OMN is asymptomatic proteinuria. As the disease progresses, serum creatinine increases. There are some clinical manifestations of impaired renal tubular function in some patients with OMN, for example, polydipsia and polyuria [12]. The volume of kidneys is normal in some patients, but there are also reports of decreased renal size. Regarding our patient, proteinuria was the first clinical manifestation, and two years later serum creatinine increased. After admission, we found that some indicators reflecting renal tubular function were also increased, for example IgG and β_2 MU, and not just proteinuria and serum creatinine. In the present patient, the specific gravity of urine was lower than normal, which was different from other reports [13]. The size of both kidneys was smaller than normal (left 9.7×3.8 cm, right 9.0×3.1 cm), and the thickness of renal parenchyma was 1.1 cm (left) and 0.9 cm (right), respectively.

The necessary condition to diagnose OMN is that the kidney pathology examination reveals increased glomerular diameter and volume. In our patient, each of both renal tissues contained six glomeruli coming from the cortex, which met with the standards. Histopathology revealed that the average diameter of glomerulus was 1.5 times larger than the diameter of normal glomerulus and the average volume of glomerulus was 3.37 times larger than normal according to the Weibe-Gomez MGV formula $V(G)=A^{1.5}(G)\times 1.38/1.01$ (V, G, A is the abbreviation of volume, glomerulus and area). All abovementioned met the diagnostic criteria of OMN.

The cause of scarce glomeruli is not yet clearly known, including some hypotheses: the first one is that the renal embryonic gene and its product regulating the development of the kidney with the inadequate embryonic development of the nephron; others are placental shunts, intravascular coagulation, low birth weight and intrauterine growth retardation. There are also cases due to genetic disorders, like 4p monosomy, PAX-2 gene mutations and hepatocyte nuclear factor-1 (HNF-1) mutations carriers, and the mechanism is perhaps also closely related with maternal age and the intrauterine environment [14]. In order to adapt the body to discharge the metabolites, scarce glomeruli must undertake the overload of work, resulting in high pressure, high perfusion and high filtration. After a long time, the diameter and volume of glomeruli change to larger than normal to meet body needs. The result is the damage of glomerular basement membrane, development of proteinuria and decreased kidney function. All changes ultimately result in glomerular sclerosis and end-stage renal disease. In this process, not only glomerulus appears with increased volume and sclerosis, but also renal interstitial and tube beome impaired [7, 12, 15]. However, there are no any changes in glomerular mesangial cells. In our patient, the volume of glomeruli increased and the renal tube was impaired, but mesangial cells and matrix were normal.

The differential diagnosis is very important for diagnosing OMN. The increased glomeruli are always found in some other diseases in pathological diagnosis, such as obesity-related nephropathy [16, 17] and diabetic nephropathy [18, 19]. But the volume of glomeruli is no more than twice the normal, and there are special changes in the mesangial district and clinical manifestations in other organs beside the kidney. OMN belongs to the secondary focal segmental glomerulosclerosis (FSGS) [20] in pathology, and it is necessary to distinguish OMN from idiopathic FSGS. The number of glomeruli is normal and the homogeneous degree of glomerular volume is not good in idiopathic FSGS. There is always glomerular sclerosis which is helpful in the differential diagnosis [21, 22, 23].

There is no special therapeutic measure for OMN. Regading the "three high" in the pathogenesis of OMN, whether the application of ARB or ACEI drugs is effective [24, 25], there are no clinical reports, and we are also still observing effects on our patient.

In summary, reports on OMN are rare, and we do not know the exact mechanism of it. Our aim is to stimulate the majority of medical personnel to get concerned about this disease. The diagnosis and treatment of OMN need further study.

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Олигомеганефронија: приказ болесника и преглед литературе

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КРАТАК САДРЖАЈ

Увод Олигомеганефронија (ОМН) је једно од ретких конгениталних обољења бубрега код којег се јављају смањење броја нефрона и повећање запремине гломерула. Није позната учесталост појаве ОМН будући да се ово обољење тешко дијагностикује. Такође, оно не показује посебне клиничке манифестације. Једини начин дијагностиковања ОМН је на основу бубрежне патологије, тако да је нетачна дијагноза резултат необављене патологије бубрега.

Приказ болесника Код 26-годишњег мушкарца постављена је дијагноза ОМН на основу налаза протеинурије и повишених вредности креатинина у серуму. Ултразвуком је откривено да је величина оба бубрега смањена у односу на нормалне вредности. Патолошки налази су указали на смањен број и веома увећане гломеруле, што је указивало на ОМН.

Закључак ОМН је ретко обољење које је такође ретко описивано. Тачан механизам његовог настанка засада није познат. Дијагноза углавном зависи од патолошких налаза. За болеснике са ОМН главни разлози одласка лекару су протеинурија и поремећај функције бубрега. Рана дијагноза је значајна.

Кључне речи: олигомеганефронија; патологија бубрега; дијагноза

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