Arab Journal of Nephrology and Transplantation

Case Report

Rapidly Progressive IgA Nephropathy in One of a Pair of Identical Twins

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Abstract

Introduction: IgA nephropathy (IgAN) is the most common cause of primary glomerulonephritis worldwide. It was considered a benign condition for many years but long term follow up showed that it might progress to end stage renal disease (ESRD). The cause of primary IgAN is unknown and no consistent genetic abnormalities that predict the development or progression of IgAN have been identified. A variety of observations suggest an association to an unknown environmental antigen, familial clustering, or infectious agent. The patient presented here is the first report of a child with IgAN in Sudan.

Case report: a seven years old boy was referred to our center for further evaluation and management of sudden onset macroscopic hematuria and renal impairment. He was born after an uneventful pregnancy and breast fed. He developed normally and was healthy before this illness. He had eight siblings who were all healthy, including his identical twin brother. Physical examination and laboratory tests led to the diagnosis of IgAN.

The patient was treated with peritoneal dialysis and pulses of methylprednisolone for three consecutive days. He showed a remarkable response and regained normal renal function. He was then kept on alternate day's steroids, ACE inhibitors, and Azathioprine. The other twin is being closely monitored.

Conclusion: This report provides an indirect support for the hypothesis that environmental factors play a role in the pathogenesis of IgAN. However, follow up of the currently healthy twin is necessary, since affection with the disease may be expressed at a later time.

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Key words: IgA nephropathy, identical twins, macroscopic hematuria

Introduction

IgA nephropathy was first described by Berger and Hinglais in 1968 and is the most common cause of primary glomerulonephritis worldwide [1].

It was considered a benign condition for many years but long term follow up showed that it might progress to end stage renal disease (ESRD). About 30% of patients will reach ESRD after 20 years, particularly those who present with hypertension, heavy proteinuria, and/or renal insufficiency [1].

It occurs frequently in Asians and Caucasians and is relatively rare in blacks, but most clinical manifestations in the two groups are similar [2].

The cause of primary IgAN is unknown and no consistent genetic abnormalities that predict the development or progression of IgAN have been identified. A variety of observations suggest an association to an unknown environmental antigen, familial clustering, or infectious agent [2-3].

IgAN has been previously described in identical adult twin sisters who presented with microscopic hematuria and proteinuria [4]. Here we report IgAN presenting as rapidly progressive glomerulonephritis in one of identical twins.

Case Report

We present a seven years old boy who was referred to our center for further evaluation and management of sudden onset macroscopic hematuria and renal impairment of two days duration. This was followed by oliguria, general ill health, and anorexia. There was no fever or history of upper respiratory tract infection.

The patient was one of a pair of identical twins born to healthy unrelated parents. He was born after an uneventful pregnancy and breast fed. He developed normally and was healthy before this illness. He had eight siblings who were all healthy, including his identical twin brother.

On physical examination, the patient was pale and puffy. There was no skin rash and no focus of infection. He had no clinical evidence of malabsorption. He was hypertensive with blood pressure measurements above the 97th centile for his age, and his weight and height were both below the 3rd centile for his age.

Blood chemistry yielded the following results: high urea (208 mg/dl) and creatinine (3.39 mg/dl) which increased rapidly over two days (urea 427 mg/dl and creatinine 7.3 mg/dl). His hemoglobin was 7.7 gm/dl, total white blood cell count was 4,300/µl and platelets were 330,000/µl/l. His ESR was 87 mm/hr. The uric acid (5.3 mg/dl) and phosphate (4.6 mg/dl) levels were both normal, but calcium level (5.6 mg/dl) was low. Potassium level (5.6 mmol/l) was slightly raised and sodium level (132 mmol/l) was normal. The ASO titre was insignificant (<200) and the ANA, ANCA and anti-GBM antibodies were negative. Complement C3 was normal. HBsAg, anti-HCV and anti-HIV antibodies were all negative.

Urine microscopy showed uncountable RBCs and proteinuria but no white cells. The urine culture for bacteria was negative. A 24 hour urine collection yielded 350 mg of proteins per 1.73 m^2. The maximum urine output per 24 hours was low for his surface area. Renal ultrasound showed bright and bulky kidneys; there were no calculi and no obstructive changes.

Renal biopsy showed features of acute crescentic nephritis with increased mesangium and mesangial matrix. The immunoflorescence confirmed the deposition of IgA and C3 but was negative for IgG, IgM and C1q. A diagnosis of IgAN was made. Serum IgA level was 1.7 g/l for the patient and 1.9 g/l for the twin brother. Both were within the normal limits.

The patient was treated with peritoneal dialysis and pulses of methylprednisolone for three consecutive days. He showed a remarkable response and regained normal renal function. He was then kept on alternate day's steroids, ACE inhibitors, and Azathioprine.

Discussion

The prevalence of IgAN is variable among different populations; it is very common in Asia (20–40%) in contrast to the United States in which the prevalence ranges from 2% to 10% with an exception of the Native Americans in whom the reported prevalence is 38% [5]. However, the lower prevalence of IgAN in some populations may be due to a racial difference in the biopsy selection/acceptance practices.

In a previous study of glomerular disease in adult Sudanese, the frequency of IgAN was low, forming 4.7% of glomerulonephritis [6]. It is worthwhile mentioning that many children with IgAN might have been diagnosed as post infectious glomerulonephritis because of the similar manifestations and the lack of facilities for proper investigations.

The patient presented here is the first report of a child with IgAN in Sudan.

Rapidly progressive crescentic nephritis is an uncommon presentation for young children [7]. Moreover, the presentation of IgAN in one of identical twin children has not been reported before. However, IgAN has been reported in a pair of adult female identical twins; they presented with microscopic hematuria and proteinuria at 32 and 39 years of age respectively [4]. The time gap in the presentation of the latter report makes us await for any development of IgAN in our so far healthy member of the twins describe in this communication.

The cause of primary IgAN is unknown. Although it is considered a sporadic disease, its presence among certain families suggests there may be a genetic predisposition, at least in some individuals [8]. However, no consistent genetic abnormality has been identified. Few reports support the suggestion of immunogenetic factors and familial clustering in combination with unknown environmental conditions in the pathogenesis of IgAN [9].

The importance of non-genetic factors in the pathogenesis of IgAN is reflected by the recurrence of IgAN in an identical twin transplant [10]. It is also supported by the reported occurrence of IgA deficiency in only one of identical twins [11], since central MHC genes are thought to affect IgA levels in the human with reciprocal effects in IgA deficiency and IgAN [12].

Conclusion

This report supports the hypothesis of an environmental etiology of IgAN since only one of a pair of identical twins is affected. However, followa up of the currently healthy twin is necessary, since affection with the disease may be expressed at a later time.

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