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BRIEF REPORT

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IgA nephropathy presenting clinical features of poststreptococcal glomerulonephritis

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Abstract IgA nephropathy and poststreptococcal glomerulonephritis are common forms of primary glomerulonephritis in children. This paper reports a 5-year-old Omani boy who had a chance occurrence of these two different glomerular diseases. Our patient presented with clinical features of poststreptococcal glomerulonephritis and then developed recurrent macroscopic hematuria, polyarthritis, bloody diarrhea, and erythematous swelling of the penis. Renal biopsy revealed diffuse mesangial hypercellularity, with focal glomerular sclerosis, fibrous crescents, and mesangial IgA and C3 deposits, consistent with IgA nephropathy. The clinical features and differential diagnosis are outlined.

Keywords Poststreptococcal glomerulonephritis · Henoch-Schönlein purpura · Hematuria · IgA nephropathy

Introduction

IgA nephropathy is the most common form of primary glomerulonephritis [1] and accounts for 15% of children with isolated hematuria for more than a year [2]. The renal symptoms are preceded by a viral respiratory or gastrointestinal illness. There is no diagnostic laboratory test. However, serum IgA concentration may be elevated and circulating IgA-containing immune complexes may be demonstrable [3]. The diagnosis depends on a high index of clinical suspicion, demonstration of mesangial deposits of IgA in the renal glomeruli, and exclusion of diseases that can present in a similar manner. Here we report the diagnosis of IgA nephropathy in a young boy who presented initially with clinical features of poststreptococcal acute glomerulonephritis (PSAGN).

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Case report

A 5-year-old boy was hospitalized with a 1-week history of upper respiratory tract infection followed by facial swelling, pedal edema, and gross hematuria. Following this, he developed pain, swelling, and limitation of movement involving the right knee, right ankle, left elbow, and left wrist. There was no history of abdominal pain, skin rash, oliguria, or polyuria. Clinical examination had shown pallor, with mild pedal edema. Blood pressure was normal, and weight was 16.8 kg (25th percentile). There was swelling of both knee joints and tenderness of the left ankle. Systemic examination was otherwise unremarkable. Three days later, he developed tender swelling of the penis, which was erythematous. Urine output was normal but he had mild proteinuria and macroscopic hematuria. Urine cytology revealed red cell casts, inflammatory cells, and reactive kidney cells. Urine protein/creatinine ratio was 106 mg/mmol (normal 20–40 mg/mmol).

Blood investigations revealed normocytic normochromic anemia (hemoglobin 8.91 g/dl, white blood cells 4.19×10^9/l, platelets 250×10^9/l). There was an inflammatory response with a high erythrocyte sedimentation rate (ESR) of 88 mm/h and C-reactive protein (CRP) of 56 mg/l (normal <8 mg/l). Serum C3 was very low at 0.09 g/l (normal 0.79–1.52 g/l); however, serum C4 was normal (0.16 g/l). Antistreptolysin O (ASO) titer was markedly elevated [>800 IU/l (normal <200 IU/L)]. Serum albumin was 23 g/l (normal 35–50 g/l). Serum electrolytes, urea, creatinine, liver enzymes, and coagulation profile were normal. An unusual finding was the high serum IgG level (38.7 g/l) (normal 7.5–15 g/l). However, both IgA and IgM levels were normal. The child was managed as PSAGN. Frank hematuria regressed and he lost 0.6 kg in weight.

The boy presented again 4 weeks later with recurrence of macroscopic hematuria, along with bloody diarrhea without any joint symptoms. On clinical examination, he was pale, normotensive, there was no edema, and his weight was down to 15.3 kg. Follow-up investigations showed persistence of granular casts in the urine and mild proteinuria. There was normochromic normocytic anemia (hemoglobin 7 g/dl), with IgG-coated positive

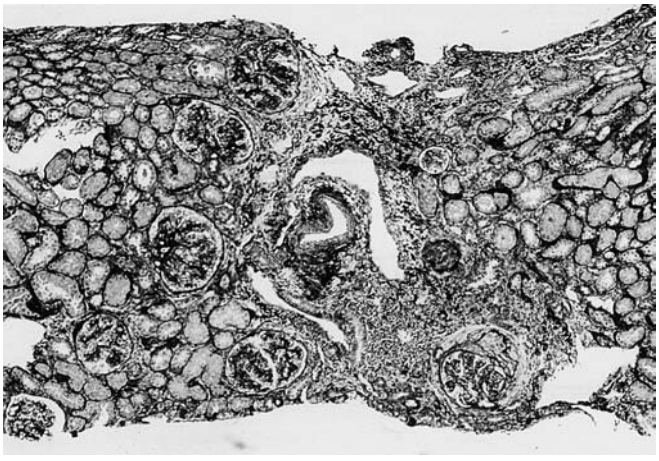

Fig. 1 Low-power view of the renal biopsy specimen showing eight glomeruli. The six on the right show mesangial hypercellularity, another (*upper left*) shows a fibrosing crescent, below which is a sclerosed tuft (H and E ×120)

Coombs′ test. Hypergammaglobulinemia (IgG 38 g/l) and low serum albumin (27 g/l) persisted. There was an increase in C3 level to 0.49 g/l and a decrease in ASO titer to 600 IU/l. Antinuclear antibodies, anti-double-stranded DNA, antineutrophil cytoplasmic antibodies, and extractable nuclear antibodies were all negative. Chest X-ray, electrocardiogram, and echocardiogram were normal. As the boy continued to have macroscopic hematuria, a renal biopsy was performed, which revealed significant renal pathology. The biopsy specimen had seven glomeruli, all showing moderate mesangial hypercellularity. One glomerulus showed a segment of capillary involvement as well. Another glomerulus had a fibrous crescent and a completely sclerosed glomerulus was also present (Fig. 1). Extraglomerular tissues were unremarkable. The immunofluorescence sample contained three glomeruli, all showing moderate amounts of IgA and C3c in the mesangium. Electron microscopy revealed three glomeruli, which showed extensive foot process fusion. Capillary walls were normal, and the mesangium expanded by cells and matrix. The latter contained numerous dense deposits with some located subendothelially. In view of the continuing symptomatology and significant renal pathology, the boy was started on oral prednisolone 1 mg/kg per day for 2 weeks and then tapered off gradually to 0.5 mg/kg on alternate days. His symptoms regressed and follow-up investigations showed normalization of hemoglobin (13.9 g/l), ESR (2 mm/h), CRP (1 mg/l), IgG (12.3 g/l), C3 (1.12 g/l), C4 (0.18 g/l), and urine protein/creatinine ratio (22 mg/mmol). The Coombs′ test had also become negative.

Discussion

Our patient presented with clinical features of PSAGN, supported by evidence of recent streptococcal infection. The low C3 was consistent with activation of the immune complex, whereas C4 levels (reflecting the classical pathway) were normal. C3 also returned to normal within 6 weeks, as is the case with PSAGN. Recurring macroscopic hematuria, however, necessitated a renal biopsy. The biopsy results revealed predominant mesangial hypercellularity with IgA and C3 deposits, narrowing the differential diagnosis to IgA nephropathy, and Henoch-Schönlein purpura (HSP) nephritis [3, 4]. The presence of a fibrous crescent in the biopsy specimen suggested that the disease antedated the PSAGN, and the latter could have activated cellular immunity and augmented renal tissue injury [5]. Patients with similar presentation, although rare, have been reported earlier [6, 7].

Transient arthritis in our patient was attributed to streptococcal infection, but he also showed evidence of vasculitis in the form of tender enlargement of the penis. Abdominal pain and bloody diarrhea also suggest HSP. However, palpable purpura seen in more than 95% of patients with HSP was not evident. Similarities between IgA nephropathy and HSP nephritis suggest that basically they are related diseases [8], since both can be encountered consecutively in the same patient, have been described in identical twins, and bear resemblance in their pathophysiology, clinical presentation, and histology.

Primary IgA nephropathy occurs at any age, with a peak incidence in the 2nd and 3rd decades of life [9]. The disease is more common in whites and Asians, and shows a male preponderance [10]. Renal manifestations commence within few days of an infection like tonsillitis, sinusitis, or gastroenteritis. Recurrent macroscopic hematuria is the hallmark of IgA nephropathy, and in a majority of patients is the only indication of renal involvement. In about 10%–15% of cases, the gross hematuria may be associated with one or more of the following: hypertension, edema, oliguria, or elevated serum creatinine level. The degree of proteinuria may vary from none to nephrotic range. The disease generally does not have any other systemic manifestations, although deposits of IgA in unaffected skin and development of mesangial IgA deposits in 35% of transplant recipients suggest systemic disease [11]. Our patient during the course of his illness developed polyarthritis, bloody diarrhea, and erythematous swelling of the penis, consistent with such systemic involvement. When IgA nephropathy is associated with involvement of other systems, as in our patient, the renal lesions are more likely to be severe than mild. With increasing severity the IgA deposits involve not only the mesangial areas, but also the capillary walls. Fibrosis with crescent formation is the residue of severe glomerular lesions. Therefore, our patient had a moderately severe histopathological abnormality with a guarded prognosis.

Although abnormality of IgA regulation has been observed in IgA nephropathy, it is still unknown if the clinical manifestations of the disorder are due to glomerular IgA deposition [12]. However, circulating IgG autoantibodies are found to activate the complement pathway and to play an important role in mediating the glomerular injury [12]. This may offer a possible explanation for the elevated levels of IgG and the positive Coombs′ test in our patient, and both resolved with clinical improvement. Both PSAGN and IGA nephropathy are common renal disorders in children, and hence it is likely that our patient had the chance occurrence of these two different glomerular diseases, with no common pathogenesis.

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