Case Report

Minimal Change Nephrotic Syndrome in a Child with Systemic Lupus Erythematosus

Abstract

Renal involvement in systemic lupus erythematosus (SLE) is well known. We present a 16-year-old boy, who was in remission on treatment for SLE for the past three years and now presented with nephrotic syndrome. The kidney biopsy was normal with the immunofluorescence revealing no deposits. He went into remission by day 9 of treatment and completed the course of treatment with prednisolone alone with no relapses. The clinical picture along with the histology and autoimmune markers for SLE indicate that he developed minimal change nephrotic syndrome that was responsive to prednisolone. It is important to be aware that minimal change nephrotic syndrome can occur in a patient as part of lupus podocytopathy and heavy immunosuppression may be unwarranted.

Keywords: *Kidney biopsy, minimal change disease, mycophenolate, nephrotic syndrome, prednisolone, systemic lupus erythematosus*

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Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder. Kidney involvement in SLE occurs in about 60% of the patients,[1,2] and can maifest with hematuria, heavy proteinuria, a nephrotic state and by renal dysfunction. Management of a child with SLE, presence of heavy proteinuria requires a kidney biopsy so that the class of lupus nephritis can be identified and appropriate treatment instituted.

Case

A 13-year-old boy presented with prolonged fever and maculopapular rashes all over the body. His weight was 43 kg and height 142 cm. His blood pressure was normal. He underwent a skin biopsy for the rash that suggested a picture like SLE. Further investigations showed hemoglobin at 11.2 gm/dl, white cell count of 9500 cells/cmm, platelets at 2.1 lakhs/microliter, and ESR at 90. His liver function tests, creatinine (0.6 mg %) and electrolytes were normal. Urine examination did not reveal any hematuria or proteinuria (urine protein/creatinine ratio 0.3 mg/mg, normal less than 0.2). C3 (18, normal range 80–178 mg/dl), C4 (5, normal range 12–42 mg/dl), anti-nuclear antibody (ANA) positivity and anti-dsDNA levels (more than 600, normal <30 IU/ml) all confirmed the diagnosis of SLE. The ultrasound scan of the kidneys was normal. He was started on mycophenolate mofetil (MMF) 750 mg twice a day and prednisolone and showed a good response in four to six months with all autoimmune markers returning to normal. He remained well in the next three years, with intermittent relapses of the rash and joint pains which were treated with repeated courses of prednisolone, while MMF dose was increased. Towards the end of the third year, while on MMF 1 gm twice a day (600 mg per sq meter per dose), he suddenly developed edema over 7 to 10 days. His weight was 66 kg and height 156 cm. His blood pressure was normal at 116/76 mmHg and there were no skin rashes or joint swellings noted. Investigations showed a hemoglobin of 10.6 gm/dl, leucocyte count of 7700/cmm with 78% neutrophils, platelet count of 3.2 lakh/cmm and a mildly raised ESR (35), low serum albumin (1 gm/dl), raised cholesterol (320 mg/dl, normal <200 mg/dl), mildly raised BUN 30 mg/dl (normal 6–24 mg/dl), a raised serum creatinine (1.4 mg %, normal <1.2 mg%) and heavy proteinuria with no hematuria (urine protein/creatinine ratio 12). In the past three years, the urine protein/creatinine ratio had remained normal. C3, C4 levels were repeated and were normal (C3 80 mg/dl, normal range 80–178 mg/dl, C4 24 mg/dl, normal range

How to cite this article: Deshpande PV. Minimal change nephrotic syndrome in a child with systemic lupus erythematosus. Indian J Nephrol 2023;33:381-3.

Received: 28-03-2022
Revised: 08-05-2022
Accepted: 13-05-2022
Published: 21-02-2023

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Access this article online

Website: https://journals.lww.com/ijon/

DOI: 10.4103/ijn.ijn_113_22

Quick Response Code:

12–42 mg/dl) and anti-dsDNA was negative. He was started on prednisolone (60 mg daily) and a kidney biopsy was performed. The kidney biopsy showed normal glomeruli with no abnormality. Immunofluorescence was negative for all immunoglobulins and C3. Electron microscopy showed no deposits and only extensive effacement of foot processes of podocytes. The serum creatinine improved to normal (0.7mg %) in the next three to four days. After nine days of prednisolone, he had shown a good response with disappearance of the edema and urine protein/creatinine ratio being 0.5 with the eventual weight of 60 kg. He completed six weeks of daily prednisolone and the prednisolone dose was then tapered off over the next three months. He remains well with no further proteinuria or relapses at a follow-up of three months after stopping prednisolone.

Discussion

Lupus nephritis is seen in 60% of the patients of SLE at presentation. In patients who do not show kidney involvement, it becomes apparent later in about 30%–48% of patients.[3] There was no evidence of renal involvement at presentation in our patient. He was started on MMF and the renal parameters were monitored throughout the next three years. The dose of MMF had to be increased for frequent relapses of rashes and joint pains needing repeated courses of steroids. Interestingly, he developed nephrotic syndrome three years after the diagnosis of SLE.

He was biopsies with the expectation that the kidney biopsy would show class 3, 4 or 5 of lupus nephritis on histology. However, to our surprise, the light microscopy was normal with the glomeruli showing no evidence of proliferation or capillary loop thickening. Immunofluorescence was negative for IgG, IgA, IgM and C3. This was also inconsistent with a diagnosis of lupus nephritis. Electron microscopy only showed extensive effacement of foot processes of podocytes with no deposits or features of membranous nephropathy.

Clinically, the proteinuria settled to normal within nine days of treatment with oral prednisolone and disappearance of edema. The clinical picture along with histology and autoimmune markers indicate that he had developed minimal change nephrotic syndrome and not lupus nephritis. Minimal change nephrotic syndrome had been described rarely in SLE earlier but has later been considered as a separate entity called lupus podocytopathy. It was often the presenting feature of SLE or associated with a flare-up of SLE. Hertig *et al*.[4] reviewed 11 patients with SLE and nephrotic syndrome, concluding that in nine patients, it was associated with a flare-up of SLE and was independent of a flare-up in only two patients. Some patients showed minimal change disease (MCD), while others showed focal segmental glomerulosclerosis (FSGS). Matsumura *et al*.[5] described three patients with SLE presenting with minimal change nephrotic syndrome. Dube *et al*.[6] showed that in seven patients of SLE with minimal change disease, five had electron dense deposits in the mesangium while only two had no deposits or mesangial expansion. Aly *et al*.[7] presented an interesting case of a girl who presented seven years after the diagnosis of SLE with minimal change nephrotic syndrome. She had received rituximab for the initial diagnosis and had been in remission. Her biopsy also showed normal glomeruli and she responded well to steroids. They believed that lupus podocytopathy could present many years later as minimal change disease. In a large study of patients with lupus podocytopathy, it was noted that out of 50 patients diagnosed with lupus podocytopathy, 13 had minimal change disease while most of the patients had mesangial deposits. Forty-seven patients responded well to steroids.[8]

In the description of two cases with lupus podocytopathy in 2016 from India, the authors presented a 22-year-old woman and a 36-year-old man who presented with features of SLE and nephrotic syndrome.[9] While the serology was positive, the histology showed no immune deposits and they responded to steroids in four weeks. The authors cautioned that lupus podocytopathy could indicate lupus activity or flare-up. In an overview of lupus podocytopathy, the authors detailed the features of lupus podocytopathy.[10] As it is seen in 1% of lupus nephritis biopsies, they consider it to be a separate entity.

Lupus podocytopathy can show MCD, FSGS or mild mesangioproliferation (class I, class II) on histology. Those with mild mesangial proliferation show a clinical course similar to MCD. Absence of immune deposits differentiates lupus podocytopathy from class I lupus nephritis. Hematuria and hypertension are absent in lupus podocytopathy and minimal change nephrotic syndrome. Patients with FSGS have a higher incidence of hypertension and acute kidney injury on clinical presentation, more severe tubulointerstitial involvement, less likely to respond to therapy, show late remissions and generally have worse outcomes. Collapsing lesions in FSGS have the worst outcome with 50% progressing to ESRD.

Our patient satisfied all three features that were suggested for diagnosis of lupus podocytopathy. Low C3 has been described in 68% of patients with lupus podocytopathy, but it was not seen in our patient. Our patient was on an adequate dose of MMF and still developed nephrotic syndrome. The serology and clinical picture did not suggest a flare-up of SLE. He responded to prednisolone in about nine days and had remained well even after tapering off the prednisolone dose. While minimal change disease as lupus podocytopathy is clearly present, it is unusual that he developed it on an adequate dose of MMF. MMF is also used to treat minimal change nephrotic syndrome with frequent relapses, with fairly good results.[11] In conclusion, it is important to be aware that nephrotic syndrome can occur in a patient with SLE on treatment and may not

always be lupus nephritis. Lupus podocytopathy as minimal change disease will respond to prednisolone and would not need aggressive immunosuppression.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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