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Case Report

Complete remission of IgA nephropathy after bone marrow transplantation for acute myeloid leukaemia

Eun-Kyung Park, Jin-Seok Jeon, Hyun-Jin Noh, Jong-Ho Won and Hee-Sook Park

Department of Internal Medicine, University of Soon Chun Hyang School of Medicine, Seoul, Korea

Abstract

IgA nephropathy is the most common primary glomerulonephritis, but the pathogenesis of IgA nephropathy is still unclear. A 32-year-old woman was found to have IgA nephropathy and acute myeloid leukaemia. She was treated with allogenic bone marrow transplantation (BMT). After BMT, immunoflourescent staining of IgA and proteinuria disappeared. These findings suggest bone marrow cells are involved in the pathogenesis of IgA nephropathy. We herein report a case of complete remission of IgA nephropathy after BMT for acute myeloid leukaemia.

Keywords: bone marrow transplantation; IgA nephropathy

Introduction

IgA nephropathy is the most common form of primary glomerulonephritis and is defined by the deposition of IgA in the glomerular mesangium. The pathogenesis of IgA nephropathy is still unclear but immunological dysfunction seems to play an important role [1]. In particular, it was reported recently that abnormalities of bone marrow stem cells play a pivotal role in the pathogenesis of glomerular disease [2]. Moreover, increasing evidence suggests that bone marrow stem cells are important for the regeneration of renal tissue after injury [3,4]. These immunological and pathophysiological observations suggest that bone marrow transplantation (BMT) may be useful for treating IgA nephropathy. Supporting this notion is the case we describe here, where a patient with IgA nephropathy who underwent treatment with BMT for acute myeloid leukaemia also showed complete remission of her IgA nephropathy, as her mesangial IgA deposits and overt proteinuria disappeared.

Case report

A 32-year-old woman presented with dizziness, dyspnoea and easy bruising. She had no previous history of diabetes, hypertension or urinary abnormalities. On examination, she was pale and dyspnoeic without pretibial pitting oedema. On admission, serum laboratory data revealed pancytopaenia with white blood cell counts of $2.2 \times 10^3/\mu L$, haemoglobin levels of 5.9 g/dL, a haematocrit value of 17.3%, platelet counts of $15 \times 10^3/\mu L$, reticulocyte counts of 4.9%, lactate dehydrogenase (LDH) levels of 47 U/L and low haptoglobin levels. Also observed were serum creatinine levels of 0.7 mg/dL, blood urea nitrogen levels of 10.5 mg/dL, total protein levels of 6.3 g/dL and albumin levels of 3.7 g/dL. Moreover, urinalysis on admission revealed 1+ proteinuria and the presence of numerous red blood cells/high power field. Serum liver function tests, prothrombin time (PT) and partial prothrombin time (PTT) were normal.

Additional studies revealed depressed complement component 3 (C3) levels of 66 mg/mL, normal complement component 4 (C4) levels of 22 mg/mL, IgG levels of 17 mg/dL, IgA levels of 242 mg/dL, IgM levels of 117 mg/dL, antinuclear antibodies (ANA) displaying a 1:40 nuclear dot pattern and urinary protein levels of 1235 mg/day. A bone marrow biopsy was performed, the results of which revealed acute erythroleukaemia (AML M6). A renal biopsy showed focal segmental mesangial proliferation and moderate expansion of the mesangial matrix with red blood cells and pigment casts. Immunofluorescence (IF) analysis revealed granular mesangial IgA and C3 deposition that was consistent with IgA nephropathy (Figure 1). After remission was achieved with a course of induction therapy, the patient completed one cycle of consolidation chemotherapy with high-dose cytarabine and idarubicin. After busulfan and cyclophosphamide conditioning therapy, she was treated with allogenic BMT using cells from her HLA-identical brother. Her clinical course was complicated by graft-versus-host disease (GVHD) after 1 month, which was treated with cyclosporine and prednisolone.

Seven weeks after BMT, urinalysis revealed a drop in urinary protein levels to 312 mg/day and only 1–4 red blood cells/high power field were observed. A second renal biopsy

Correspondence and offprint requests to: Jong-Ho Won, Department of Internal Medicine, University of Soon Chun Hyang School of Medicine, 657 Hannam Dong, 140-743 Seoul, Korea. Tel: +82-2-709-9203; Fax: +82-2-792-5812; E-mail: jhwon@hosp.sch.ac.kr

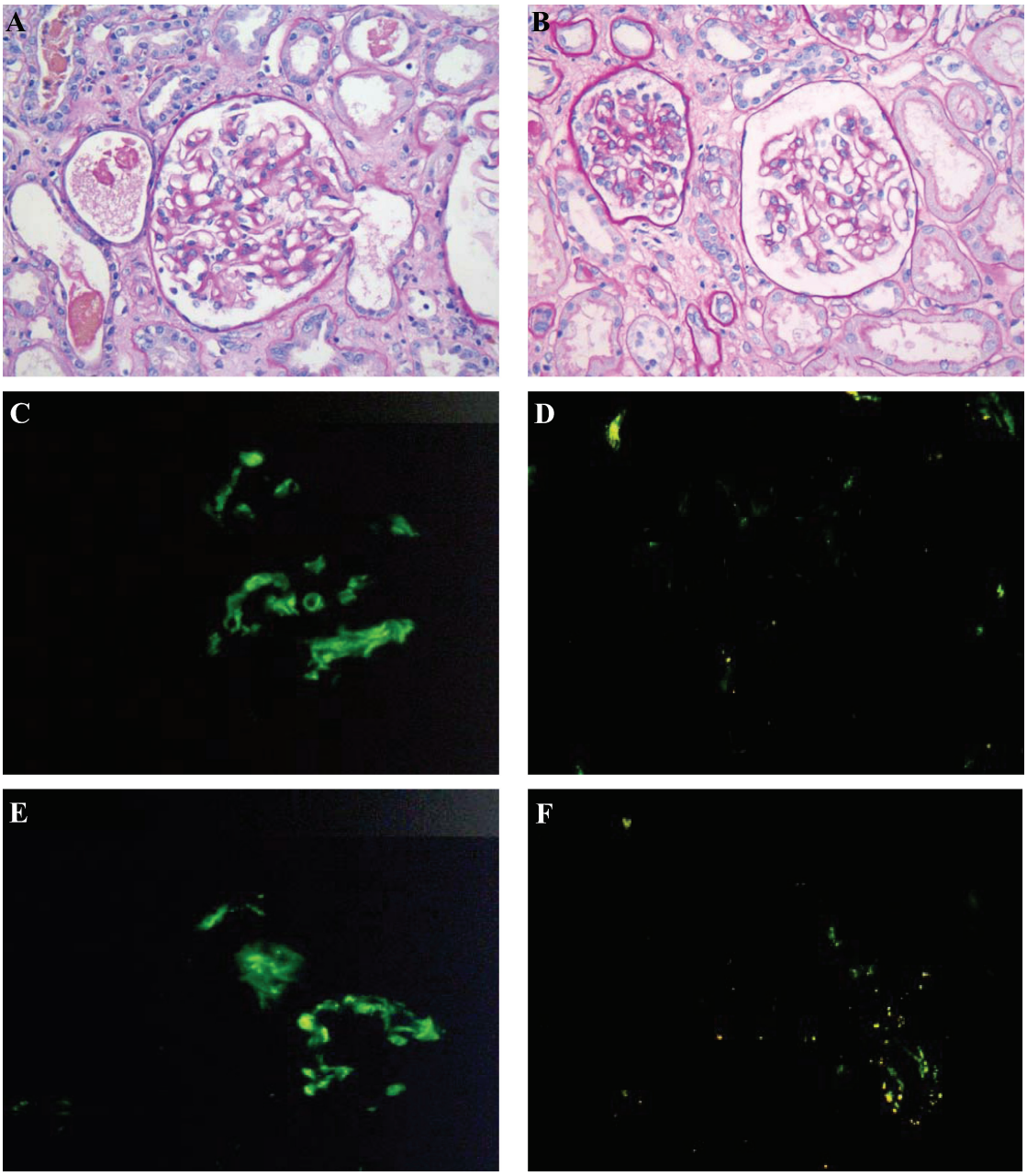

Fig. 1. The first renal biopsy specimen obtained upon admission showed focal segmental mesangial proliferation and moderate mesangial expansion (**A**) with strong mesangial immunofluorescent staining of IgA (**C**) and C3 (**E**), which is consistent with IgA nephropathy. The second renal biopsy taken 14 months after haematopoietic stem cell transplantation showed decreased mesangial cellularity and mesangial matrix expansion (**B**) with trace mesangial immunofluorescent staining of IgA (**D**) and C3 (**F**) (periodic acid-Schiff staining; original magnification ×400).

was performed 14 months after BMT. Light microscopy showed decreased mesangial cellularity and trace mesangial IF staining of IgA and C3 (Figure 1). Upon electron microscopy, the dense mesangial deposits seen in the previous biopsy before the HSCT were almost completely absent. At the last follow-up, the patient was in complete haematological remission with serum creatinine levels of 0.9 mg/dL and urinary protein excretion of 50 mg/day without haematuria.

Discussion

Although many studies on IgA nephropathy have been reported, the pathogenesis of this disease is unclear and an effective treatment for this disease is not yet available [5]. However, in 1997, Sakai published a case report of a patient with IgA nephropathy and chronic myeloblastic leukaemia whose BMT not only cured the leukaemia but also eliminated the mesangial IgA deposits [6]. Moreover, Imasawa

et al. reported that the transfer of bone marrow stem cells from IgA nephropathy-prone mice induced IgA deposition in the glomeruli of normal mice and that transplantation of bone marrow from normal mice into IgA nephropathy-prone mice attenuated their renal lesion and reduced the degree of albuminuria and their serum macromolecular IgA levels [7]. Moreover, a recent report by Suzuki *et al*. has suggested that IgA-producing bone marrow cells may drive the development of IgA nephropathy [8]. These findings suggest that bone marrow stem cells are involved in the pathogenesis of IgA nephropathy. Notably, autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus are currently being treated by BMT [9]. Two possible mechanisms may explain the therapeutic effect of BMT on glomerular disease. One is that the BMT replaces the recipient's destructive immune cells with the donor's bone marrow cells. The other possible mechanism is that the reconstitution of glomerular cells with donor bone marrow cells helps to attenuate the glomerular lesions in IgA nephropathy [10]. In our case, we performed fluorescent *in situ* hybridization (FISH) analysis after BMT but could not detect Y-chromosome-positive cells in the kidney tissue (data not shown). This finding suggests that the BMT-mediated attenuation of glomerular injuries is driven by the reconstitution of the immune system rather than the reconstitution of the glomerulus.

Our case suggests that BMT may be a new therapeutic strategy for the treatment of IgA nephropathy. It also suggests a novel approach to the study of IgA nephropathy pathogenesis. However, the use of allogenic BMT to treat nonmalignant disorders must be very carefully considered in view of its associated toxicity and potential morbidity. Indeed, it may be advisable to consider less aggressive non-myeloablative BMT for the treatment of IgA nephropathy, as this may reduce renal damage while inducing less non-relapse mortality.

Conflict of interest statement. None declared.

References

1. Lai KN, To WY, Li PK *et al*. Increased binding of polymeric lambda-IgA to cultured human mesangial cells in IgA nephropathy. *Kidney Int* 1996; 49: 839–845
2. Imasawa T, Utsunomiya Y, Kawamura T *et al*. The potential of bone marrow-derived cells to differentiate to glomerular mesangial cells. *J Am Soc Nephrol* 2001; 12: 1401–1409
3. Abbattista MR, Schena FP. Stem cells and kidney diseases. *Minerva Med* 2004; 95: 411–418
4. Schachinger V, Zeiher AM. Stem cells and cardiovascular and renal disease: today and tomorrow. *J Am Soc Nephrol* 2005; 16(Suppl 1): S2–S6
5. Donadio JV, Grande JP. IgA nephropathy. *N Engl J Med* 2002; 347: 738–748
6. Sakai O. IgA nephropathy: current concepts and future trends. *Nephrology* 1997; 3: A2–A3
7. Imasawa T, Utsunomiya Y. Stem cells in renal biology: bone marrow transplantation for the treatment of IgA nephropathy. *Exp Nephrol* 2002; 10: 51–58
8. Suzuki H, Suzuki Y, Aizawa M *et al*. Th1 polarization in murine IgA nephropathy directed by bone marrow-derived cells. *Kidney Int* 2007; 72: 319–327
9. Krance R, Brenner M. BMT beats autoimmune disease. *Nat Med* 1998; 4: 153–155
10. Imasawa T. Roles of bone marrow cells in glomerular diseases. *Clin Exp Nephrol* 2003; 7: 179–185

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