Sirolimus S

Glomerulosclerosis and proteinuria: 5 case reports

Five patients developed proteinuria and four patients developed biopsy-proven focal segment glomerulosclerosis (FSGS) during immunosuppression therapy with sirolimus.

Patient 1, a 34-year-old man with FSGS evolved to end-stage kidney disease, underwent kidney allograft transplantation and started receiving an immunosuppressive regimen of sirolimus 10 mg/day, gradually adjusted to a target concentration of 6 to 12 ng/mL, basiliximab, mycophenolate mofetil and prednisone. Fourteen months later, he developed proteinuria (3.2 g/day) with a decreased serum albumin level (2.8 g/dL) and an elevated creatinine level of 1.8 mg/dL (baseline 1.3 mg/dL). Physical examination showed mild hypertension and mild oedema of his lower limbs. Graft biopsy revealed recurrent FSGS. Two months later, he had a serum creatinine level of 2.8 mg/dL and a second graft biopsy showed recurrent FSGS. He received pulse corticosteroid therapy without a satisfactory response. His serum creatinine level increased to 5.2 mg/dL and his proteinuria worsened (13 g/day). Sirolimus was replaced by ciclosporin and mycophenolate mofetil and his serum creatinine level decreased to 1.4 mg/dL and his proteinuria decreased to 6 g/day. However, he experienced further deterioration and, 2 years after transplantation, he started undergoing haemodialysis.

Patient 2, a 32-year-old man with end-stage kidney disease, underwent kidney allograft transplantation and started receiving an immunosuppressive regimen of sirolimus 10mg [*frequency not stated*] for 3 days, reduced to 5mg [*frequency not stated*] to achieve a target concentration of between 6 and 12 ng/dL, in addition to basiliximab, tacrolimus and prednisolone. One month after transplantation, his serum creatinine level increased from 1.3 to 1.6 mg/dL and a dipstick test showed proteinuria and a 24-hour protein level of 1g. A graft biopsy showed acute rejection and he received methylprednisolone. After 26 months, he was admitted with graft impairment and an elevated serum creatinine level (2.4 mg/dL), proteinuria (+++) and 3.1g of protein in 24-hour urine. A graft biopsy revealed FSGS. Sirolimus was replaced by mycophenolate mofetil and his serum creatinine level stabilised at 2.4 mg/dL and he had a 24-hour urinary protein level of 4g.

Patient 3, a 36-year-old man with end-stage kidney disease, underwent kidney allograft transplantation and started receiving basiliximab, ciclosporin, and azathioprine that was replaced by mycophenolate mofetil due to high liver enzyme levels. Ten months after transplantation, he developed graft impairment and he received pulse corticosteroid therapy and ciclosporin was replaced by sirolimus 5 mg/day; he had a serum creatinine level of 2.1 mg/dL. Three months later, he developed proteinuria (12 g/day) and his graft function deteriorated with a creatinine level of 2.4 mg/dL. A graft biopsy revealed FSGS. Sirolimus was discontinued and his serum creatinine level and proteinuria decreased to 2.2 mg/dL and 5 g/day, respectively.

Patient 4, a 32-year-old man with end-stage kidney disease, underwent kidney allograft transplantation and started receiving basiliximab, corticosteroid, ciclosporin and azathioprine. However, on postoperative day 3, he developed fever, oliguria and a lag in serum creatinine decrease. He received an empirical corticosteroid pulse and a graft biopsy showed thrombotic microangiopathy, which was attributed to ciclosporin. Ciclosporin was replaced by sirolimus 5 mg/day and azathioprine was replaced by mycophenolate mofetil, with a fair response. Three months after transplantation, he was admitted with proteinuria (13.8 g/day), lower limb oedema and hypoalbuminaemia (2.4 g/dL). A graft biopsy showed a picture of FSGS. Sirolimus was replaced by tacrolimus and, 2 months later, his serum creatinine level was 1.3 mg/dL, his proteinuria had improved (4 g/day) and his serum albumin level had increased (3.1 g/L).

Patient 5, a 37-year-old woman with membranoproliferative glomerulonephritis (MPGN) evolved to end-stage kidney disease, underwent kidney allograft transplantation and started receiving an immunosuppressive regimen of basiliximab, sirolimus 10 mg/day, mycophenolate mofetil and prednisone. Six months after transplantation, she developed graft impairment with an elevated serum creatinine level (1.7 mg/dL). Physical examination revealed mild lower limb oedema. Her urinalysis showed proteinuria (+) and she had a serum albumin level of 3 g/dL. Graft biopsy showed recurrent MPGN and borderline rejection. She received pulse corticosteroids with partial improvement. However, her graft function continued to worsen and, 8 months later, she was admitted with a serum creatinine level of 6 mg/dL and worsened proteinuria (8 g/day). Sirolimus was stopped and her graft function improved with a decrease in her serum creatinine level and proteinuria to 2.7 mg/dL and 3.5 g/day, respectively.

Sabry AA, et al. Is sirolimus a nephrotoxic drug? A report of five cases. Transplantation Proceedings 39: 1406-1409, No. 5, Jun 2007 - Egypt 801071845