Successful Treatment of Rituximab-Refractory Waldenstrom Macroglobulinemia-Related Kidney Damage With Bruton Tyrosine Kinase Inhibitor

To the Editor: At present, the clinical pathology and treatment prognosis of Waldenstrom macroglobulinemia (WM)-related kidney damage are still not very clear.

We reported for the first time that a patient with rituximab-refractory WM with cryoglobulinemia-related kidney damage who was treated with ibrutinib got rid of dialysis. Both MYD88 and CXC chemokine receptor 4 of the patient were mutated, after 3 cycles of rituximab, cyclophosphamide, and dexamethasone treatment. No kidney function was found with significant improvement, but after the addition of ibrutinib, the patient's symptoms improved significantly, he got rid of dialysis, and serum cryoglobulin turned negative, revealing a good response to ibrutinib (Case report, Supplementary Figures S1 and S2).

WM/lymphocytic lymphoma is a clinically rare lymphoproliferative disease that has been reported to occur in 3 to 4 cases per million individuals per year, most often in Caucasians.[1,2] It is characterized by the presence of monoclonal IgM paraprotein and clonal lymphoplasmacytic cell bone marrow infiltration.[3] Prompt treatment is needed when symptoms appear, especially complicated with kidney damage. Current treatment options include alkylating agents, corticosteroids, proteasome inhibitors, and anti-CD20 monoclonal antibodies. Owing to the extensive and repeated use of rituximab and rituximab-based combination therapies in WM, rituximab-based resistance has been increasingly observed, limiting its use. Ibrutinib is a first-rate, potent, irreversible, covalently bound oral inhibitor of Bruton's tyrosine kinase that has recently revealed significant single-agent activity in several B-cell lymphoma subtypes.

A phase 3 trial of ibrutinib for rituximab-refractory WM (iNNOVATE [an open-label substudy of an international, multicentre, phase 3 trial]) found that in a median follow-up period of 18.1 months (interquartile range: 17.5–18.9), the proportion of patients in overall remission was 28 of 31 (90%). The estimated 18-month progression-free survival rate was 86% (95% confidence interval: 66–94).[4] In another prospective phase 3 trial, the 30-month progression-free survival rate in combination with ibrutinib and rituximab was found to be superior to placebo and rituximab (82% and 28%, respectively).[S13]

We reported for the first time that a patient with rituximab-refractory WM with cryoglobulinemia-related kidney damage who was treated with ibrutinib got rid of dialysis. Use of ibrutinib may be one of the alternatives for rituximab-refractory WM with severe kidney impairment (Supplementary Table S1).

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Case report.

Supplementary References.

Figure S1: Morphologic features of membranoproliferative glomerulonephritis on renal biopsy of the patient with Waldenstrom's macroglobulinemia. (A) Mesangial cells were severely proliferated and lobulated, and mesangial matrix was moderately increased (asterisks; periodic acid–Schiff [PAS], original magnification ×400). (B,C) Deposits were observed in mesangial, subcutaneous, and subepithelial areas (periodic acid-silver metheramine [PASM]; B, original magnification ×400; C, original magnification ×600). (D) Deposits stained with IgM in the mesangial area and paramesangial area on immunofluorescence (original magnification ×400). (E,F) On electron microscopy, electron-dense deposits were observed in the subendothelial, mesangial area and medial of basement membrane. Foot processes revealed diffuse fusion (original magnification ×2500).

Figure S2: Serum creatinine and urine volume levels before and after the start of ibrutinib. Serum creatinine and urine volume levels both normalized after initiation of ibrutinib. CP: cyclophosphamide; DXM: dexamethasone; THD: thalidomide.

Table S1: Key teaching points.

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