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Immunotactoid Glomerulopathy Successfully Treated with Mizoribine

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Abstract

Immunotactoid glomerulopathy and fibrillary glomerulonephritis are forms of nephritis characterized by the presence of electron-dense deposits with a nonbranching fibrillary structure similar to that of amyloids in the extracellular matrix within the glomeruli under electron microscopy. Treatment options for patients with nephrotic syndrome include steroids and other immunosuppressants, plasmapheresis, or renal transplantation. However, no standard treatment method has been established. Because mizoribine has relatively few adverse effects compared with many of the immunosuppressants in general clinical use, it is appropriate for outpatient treatment of immunotactoid glomerulopathy.

Keywords

Mizoribine; Immunotactoid glomerulopathy; Nephritis

Introduction

Immunotactoid glomerulopathy (ITG) and fibrillary glomerulonephritis are forms of nephritis characterized by presence of electron-dense deposits with a nonbranching fibrillary structure similar to that of amyloids in the extracellular matrix within the glomeruli under electron microscopy, which are negative for amyloid staining and positive for immunoglobulin and complement [1, 2]. ITG is described as exhibiting a microtubular structure that has a central core of fibers with a width of 30 to 50 nm, while fibrillary glomerulonephritis has fibers with a diameter of 18 to 22 nm, larger than that of amyloid fibers [3].

Proteinuria is usually present, and nephrotic syndrome (NS) is observed in many cases. It often occurs in combination with lymphoproliferative disorders, and if an underlying condition is present, this receives priority in treatment. Treatment options for patients with NS include steroids and other immunosuppressants, plasmapheresis, or renal transplantation. However, no standard treatment method has been established. Here, we describe a patient with ITG treated with mizoribine a treatment that has not been previously reported for this condition who achieved remission of NS.

Case Report

An 82-year-old woman with a history of bilateral pedal edema and weight gain for 6 months was admitted for NS. The results of her physical examination were normal. Laboratory tests revealed a serum creatinine level of 1.23 mg/dL, indicating kidney dysfunction, as well as an albumin level of 2.3 g/dL and proteinuria (5 g/day), indicating NS; hypocomplementemia also was present, but there was no cryoglobulinemia. There were no indications of paraproteinemia or a lymphoproliferative disorder.

A kidney biopsy subsequently was performed. Nodules and an increase in the amount of the mesangial matrix were seen in the glomeruli accompanied by cellular proliferation (Figure 1). The result for Congo red staining was negative. The deposits were immunoglobulin G dominant, with staining for both κ and λ light chains. C3 deposits also were seen in the glomeruli. The subendothelial deposits demonstrated a microtubular structure that had a central core that was slightly curved with a width of 30 to 50 nm (Figure 2). Based on these findings, ITG was diagnosed.

Predonine (30 mg/day) did not bring about any change in the patient's proteinuria; thus, after 1 month, mizoribine (150 mg/day) was added. Two months later, the patient's proteinuria had decreased to 1 g/day, her albumin level was 2.9 g/dL, and her pedal edema also had improved, at which point, she was discharged.

Three years after onset, there was no NS recurrence, and her proteinuria was steady at 0.5 g/day by treatment with predonine (5mg) alone (Figure 3).

Discussion

Mizoribine not only has potential for treatment of ITG, but also has relatively few adverse effects compared with other immunosuppressants. Mizoribine is an antimetabolic immunosuppressant that was developed in Japan over 20 years ago. It is excreted via the kidneys, and through its mechanism of action involving selective inhibition of inosine monophosphate dehydrogenase the main enzyme in the de novo pathway involved in purine biosynthesis nucleic acid synthesis is suppressed [4]. This de novo pathway for purine biosynthesis is present mainly within lymphoid immune cells, indicating that the action of mizoribine is more lymphocyte-specific compared to that of azathioprine a metabolic immunosuppressant that inhibits both this de novo pathway as well as the salvage pathway. Details of the pathology of ITG remain unknown, but patients often have a lymphoproliferative disorder, suggesting that mizoribine may be effective due to its lymphocyte-specific action [5]. Proliferative lesions associated with nodular lesions have been reported to respond to steroids. However, the patient in the present case did not respond to steroid treatment, and only started to improve after mizoribine was added [6].

For patients who develop ITG after age 65 years of age, mizoribine is more appropriate than cyclosporine as the first-choice immunosuppressant for use in combination with steroids. Cyclosporine is known to be clinically effective for treatment of steroid-dependent NS. However, in intractable cases, cyclosporine withdrawal may prove difficult, requiring long-term administration. In such cases, the adverse effects of cyclosporine are a cause for concern. High-dose administration of mizoribine before starting cyclosporine is reportedly effective for avoiding cyclosporine administration [7]. We have previously described a patient with steroid-dependent NS treated with long-term cyclosporine who developed purulent spondylitis [8].

Based on this case, because mizoribine has relatively few adverse effects compared with many of the immunosuppressants in general clinical use, it is appropriate for outpatient treatment of ITG.

Figures

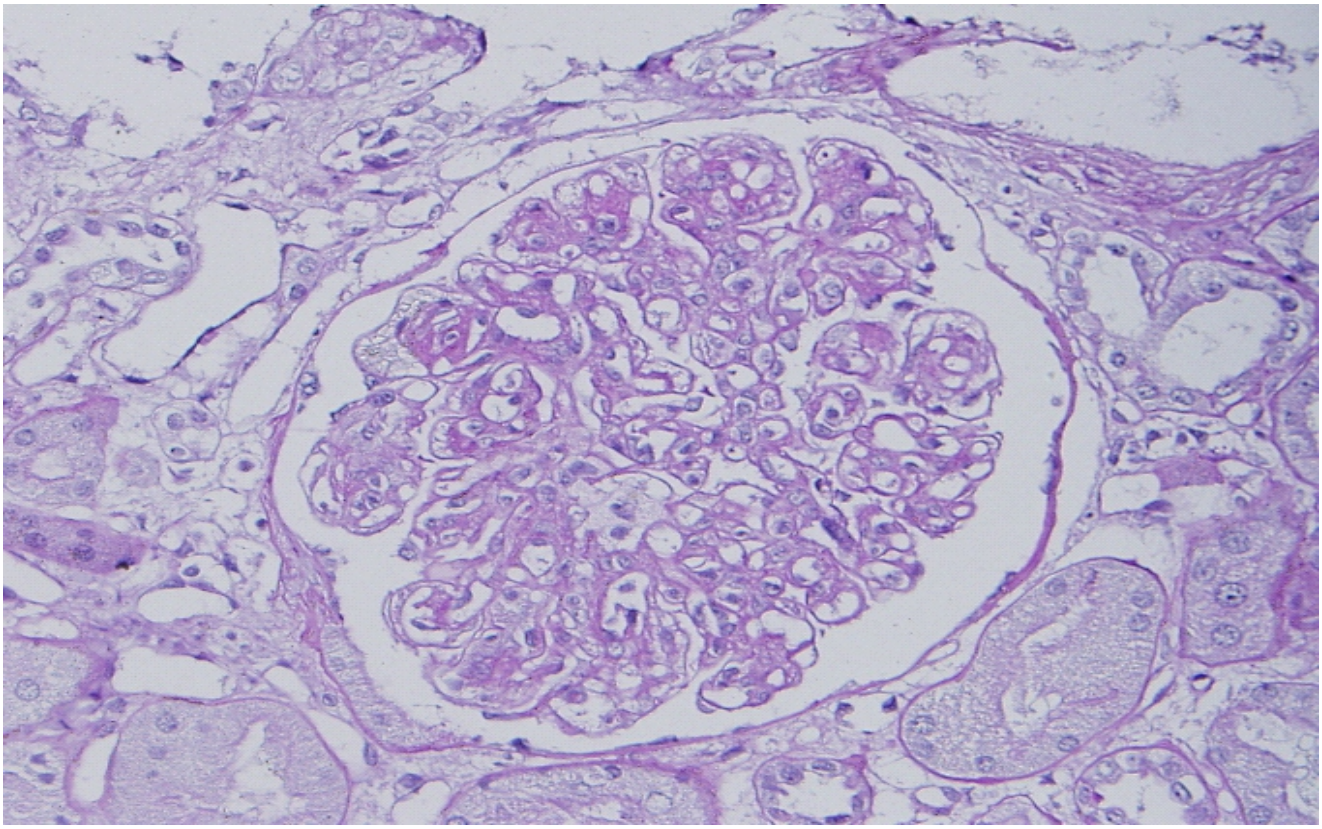
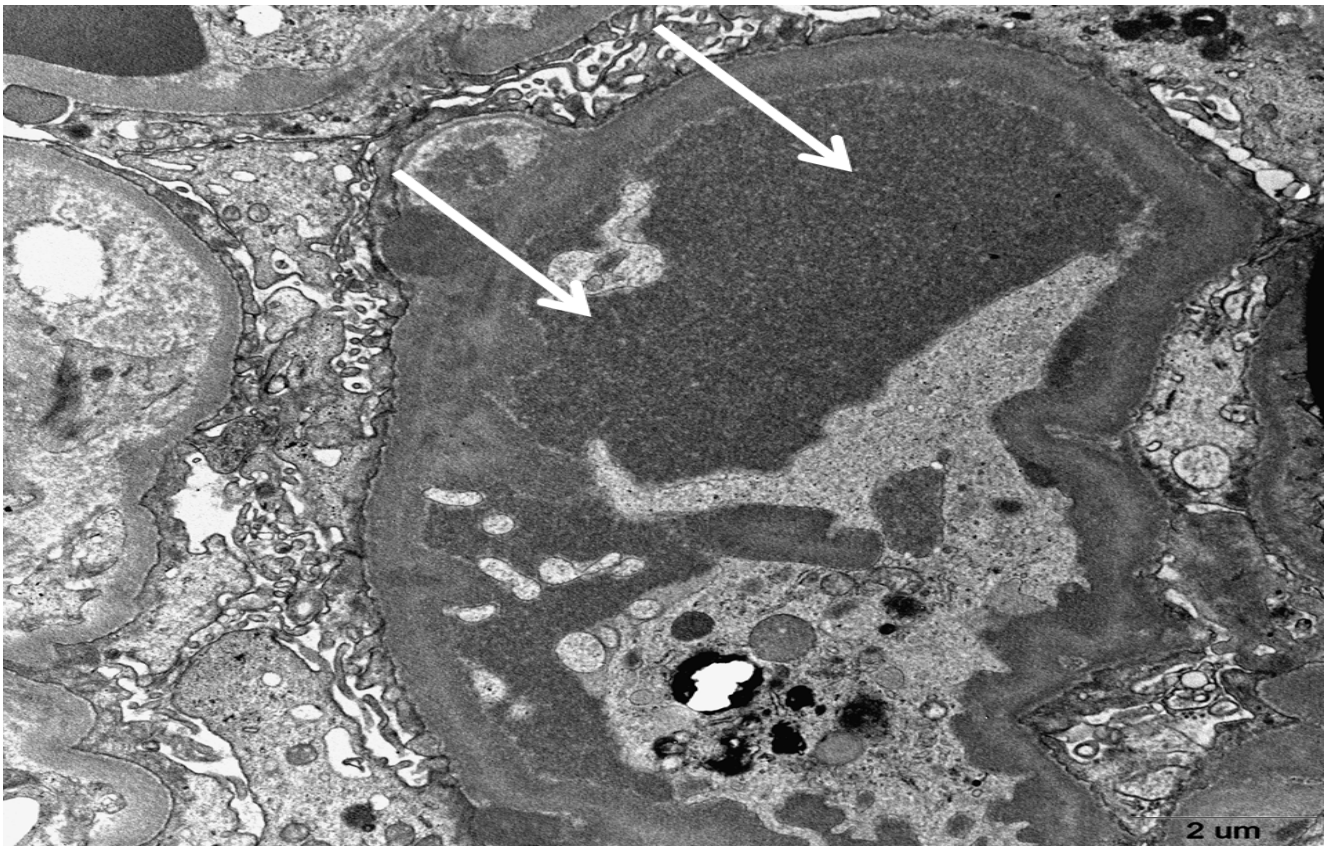


Figure 1: Light microscopic findings. Examination of the kidney biopsy showed a membranoproliferative glomerulonephritis pattern of injury with mild mesangial hypercellularity, global duplication of the glomerular basement membranes, and global large mesangial and subendothelial immune deposits (magnification ×400).



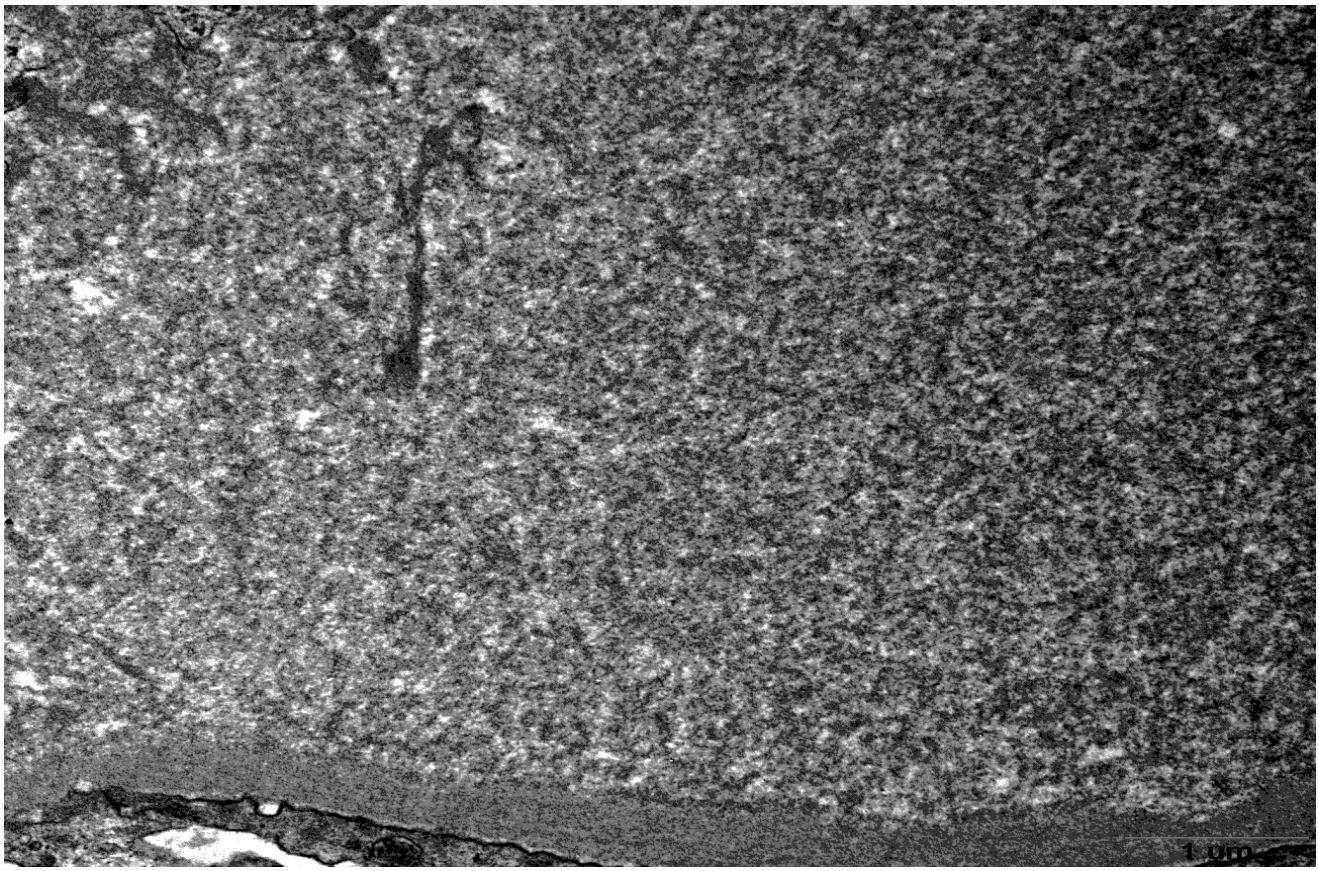


Figure 2 (A&B): Electron microscopic findings. Ultrastructural examination of the kidney biopsy showed large mesangial and subendothelial electron-dense deposits (white arrows) (A: magnification ×1850, B: magnification ×30,000).

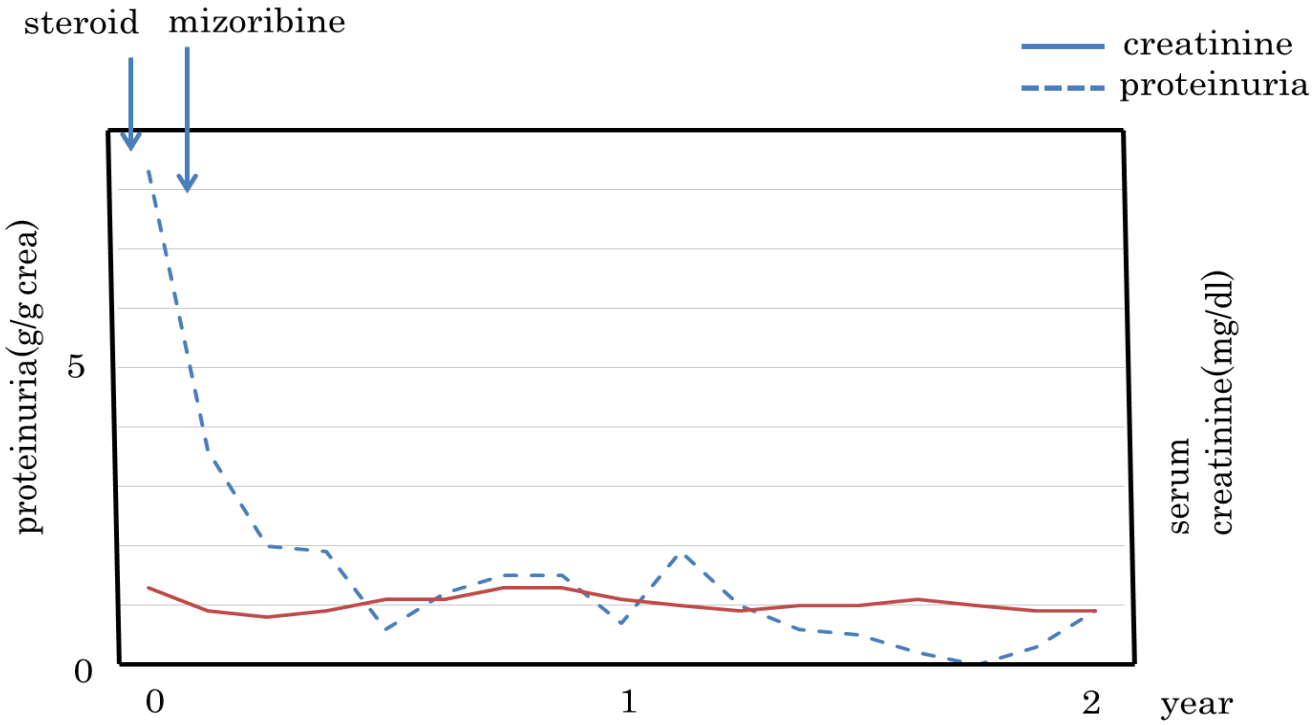


Figure 3: Treatment with predonine and mizoribine reduced the patient's proteinuria to levels between 0 and 1 g/g creatinine, with no significant change in the serum creatinine level.

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