Mizoribine induces remission of relapsed ANCA-associated renal vasculitis

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A 70-year-old woman who was diagnosed with antineutrophil cytoplasm antibody (ANCA)-associated renal vasculitis was admitted to our hospital, because of walking difficulties with muscle weakness of both lower extremities and fever with neutropenia. She was treated with 20 mg/day prednisolone and 50 mg/day cyclophosphamide (CYC). Her serum creatinine level remained the same (1.29 mg/dl) and myeloperoxidase (MPO)-ANCA was within the normal range (<10 EU). Urinalysis revealed normal red blood cell sedimentation. The ANCA-associated renal vasculitis did not relapse, but she was diagnosed with steroid myopathy and febrile neutropenia due to complication of CYC. After discontinuing CYC and tapering of prednisolone, the serum creatinine level was elevated to 1.75 mg/dl and urinalysis revealed haematuria and red blood cell casts. A high MPO-ANCA titre (24 EU) indicated relapse of renal vasculitis. Mizoribine therapy was started at a dose of 50 mg/day (once each day) together with 15 mg/day prednisolone. Four weeks later, the serum creatinine level and MPO-ANCA titre declined to 1.29 mg/dl and <10 EU, respectively (Figure 1). Urinalysis 8 weeks later showed that haematuria and red blood cell casts had disappeared.

Mizoribine is a purine synthesis inhibitor that has an immunosuppressive effect equivalent to that of azathioprine, but it is safer than other immunosuppressive drugs [1,2]. Mizoribine has recently been proved clinically effective and safe for the treatment of nephrotic syndrome [3], immunoglobulin-A nephropathy [4] and lupus nephritis [5]. For ANCA-associated renal vasculitis, it was reported that mizoribine was useful as a pre-emptive treatment to prevent relapse, but less effective as a treatment after relapse [6]. In contrast, we found that mizoribine was very effective against the relapse of ANCA-associated renal vasculitis, at least in this patient.

Mizoribine, in the range 0.1–5 μg/ml, inhibits human mixed-lymphocyte reaction at rates of 36.4–62.2%, with 50% inhibition at a concentration of ~1 μg/ml [2]. On the other hand, liver dysfunction and thrombocytopenia developed with a trough level of >5 μg/ml [2]. Therefore, blood levels should be monitored to determine optimal and safe dosages of mizoribine, particularly when renal dysfunction is present. The concentrations of mizoribine in this patient are shown in Figure 2. The trough level in this patient was 0.35 μg/ml and the Cmax was 1.31 μg/ml. We therefore surmised that these blood levels of mizoribine were adequate to achieve the remission of relapsed ANCA-associated renal vasculitis.

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Fig. 1. Serum creatinine level, dose of prednisolone, during mizoribine therapy.
In conclusion, it is important to monitor the blood level in order to determine optimal dosages of mizoribine. Mizoribine will be useful not only as a preemptive treatment to prevent relapse, but as also an aggressive strategy to induce the remission of relapsed ANCA-associated renal vasculitis.

Conflict of interest statement. None declared.

References


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