Mod Rheumatol (2006) 16:264–266
DOI 10.1007/s10165-006-0494-2

CASE REPORT

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Tacrolimus treatment for refractory lupus cystitis

Received: November 28, 2005 / Accepted: May 19, 2006

Abstract A 23-year-old woman presented with recurrence of lupus cystitis, which had been in remission under daily administration of a single corticosteroid over a period of 8 years. She was treated with increased doses of corticosteroid and immunosuppressants, i.e., cyclosporin, cyclophosphamide, azathioprine, and salazosulfapyridine, but the cystitis remained active. Since her condition became critical by the complication of intestinal pseudo-obstruction, tacrolimus was administered. This agent induced a remission promptly without significant adverse events in this patient, suggesting an efficacy to lupus cystitis refractory to corticosteroid and other immunosuppressants.

Key words Corticosteroid · Cyclosporin · Lupus cystitis · Refractory · Tacrolimus

Introduction

Lupus cystitis is a relatively rare complication of systematic lupus erythematodes (SLE), which usually responds to corticosteroid treatment. However, severe complications, such as hemorrhage and perforation of the intestinal tract, may occur in limited cases unresponsive to corticosteroids and can lead to an unfavorable prognosis. Here we describe our experience of such a case in which lupus cystitis was unresponsive to corticosteroids and immunosuppressants, and presented intestinal pseudo-obstruction (IPO).

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Case report

A 23-year-old Japanese woman, diagnosed as having SLE at the age of 15, remained in a stable condition under 10 mg of prednisolone daily until vomiting and diarrhea developed. Examinations revealed ascites, bilateral hydronephrosis, and thickened bladder wall. An endoscopic biopsy of bladder mucosa confirmed the diagnosis of lupus cystitis. The patient was then treated with increased doses of corticosteroid; however, cystitis became recrudescent on tapering of the drug. The patient at first achieved disease control with an addition of cyclosporin; however, her condition again deteriorated. She was then admitted to Kurume University Hospital. On admission laboratory findings included elevated antinuclear antibody (×160, nucleolar/homogeneous type) and low complement (C3 of 49 [>72], C4 of 8 [>11]). Abdominal ultrasonography revealed ascites, thickening of the bladder wall, and bilateral hydronephrosis (Fig. 1a). She was given azathioprine, salazosulfapyridine, and cyclophosphamide; however, there was no improvement and she presented a marked abdominal distension, anorexia, and constipation. An abdominal X-ray showed air-fluid collection inside then intestine (Fig. 2), suggesting intestinal pseudo-obstruction (IPO) caused by SLE. Since abdominal distension worsened despite total parenteral nutrition, tacrolimus was initiated. Abdominal distension subsided within 7 days of the treatment, as did ascites and hydronephrosis (Fig. 1b). The patient is still in a stable condition four years later (Fig. 3).

Discussion

Lupus cystitis is a rare complication of SLE, presenting nausea, vomiting, and ileus.[1] Hydronephrosis is common in lupus cystitis, probably due to fibrosis of the ureterovesical junction and spasm of the detrusor muscle. Intestinal pseudo-obstruction has been reported to complicate lupus cystitis.[2] Most patients with lupus cystitis respond to

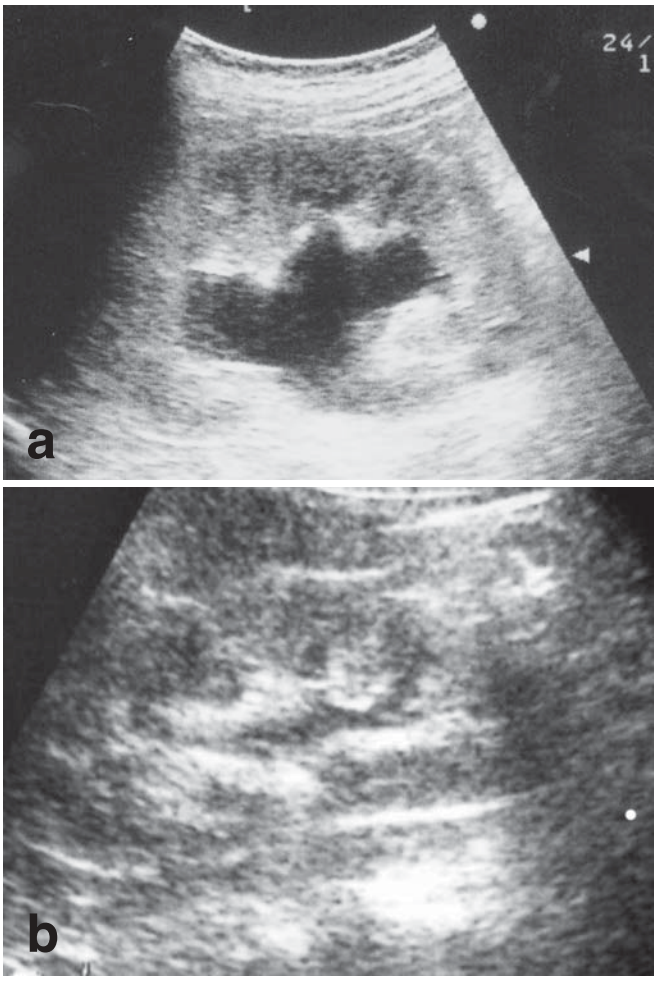
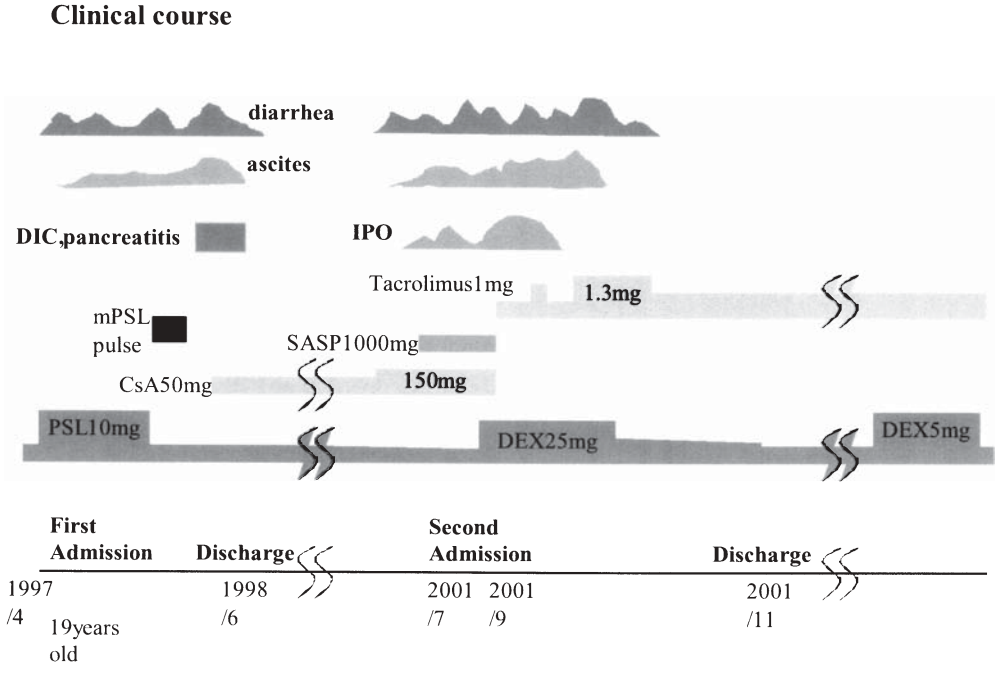


Fig. 1. a. Severe hydronephrosis is seen on ultrasonography. **b** After inducing tacrolimus, hydronephrosis improved remarkably

Fig. 2. Severely dilated bowel with air-fluid collection is seen on abdominal X-ray. This is thought to be intestinal pseudo-obstruction

Fig. 3. Clinical course



corticosteroid; however, additions of immunosuppressants are required for difficult cases. More refractory cases, in which even combinations of these agents are not effective, may result in a fatal outcome due to severe complications such as intestinal tract perforation and multiorgan failure.[3,4] The present patient is one of these refractory cases in which increased doses of corticosteroid, cyclosporin, azathioprine, and salazosulfapyridine could not control the disease. Tacrolimus is another immunosuppressant known to have efficacy on several autoimmune diseases, including SLE.[5–7] Although cyclosporin and tacrolimus have the similar immunosuppressive action of antagonizing calcineurin,[8] several cases of SLE resistant to cyclosporin have been reported to present clinical improvement using tacrolimus,[5] as in our patient.

To explain the difference in immunosuppressive action between cyclosporin and tacrolimus, evidence is available showing that tacrolimus but not cyclosporin inhibits T-cell proliferation induced by cytokines (interleukin [IL]-2 and IL-7) and IL-2-induced IL-5 production by human T cells.[8–10] It is possible that these differences in immunosuppressive action on activated T cells underlie the present observation, suggesting an important role of activated T cells in the pathogenesis of refractory lupus cystitis. Although experience is still limited, tacrolimus can be a treatment option for patients with refractory lupus cystitis.

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