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Exceptional Case

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Azithromycin suppressed relapses of idiopathic nephrotic syndrome in a child

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Abstract

Long-term immunosuppressive therapy with severe adverse effects is indispensable to maintain disease remission in frequently relapsing nephrotic syndrome (NS) in children. Hence, development of new therapy with less toxicity for relapses of NS is required. We demonstrated a case of a 2-year-old boy with frequently relapsing NS, whose frequent relapses were successfully treated with azithromycin. Azithromycin treatment prevented the need for long-term immunosuppressive therapy in this case. Azithromycin could be a new treatment option for relapse of NS, with few adverse effects, in selected cases.

Key words: azithromycin, nephrotic syndrome, pediatrics, proteinuria, relapse

Introduction

Idiopathic nephrotic syndrome (NS) in children is a disease of unknown etiology in which serum proteins leak from kidney into the urine, resulting in hypoproteinemia and edema. More than 80% of NS patients are sensitive to corticosteroids at the first episode, suggesting that perturbation of immune systems is a proposed pathogenetic mechanism of NS. Corticosteroids can suppress disease activity temporarily; however, 60% of steroid-sensitive NS experiences relapses. Due to the high relapse rate, long-term immunosuppressive therapy is indispensable to maintain disease remission, especially in frequently relapsing NS. Immunosuppressive therapy including corticosteroids has serious adverse effects during the long lifetime of NS children, hence, they and their families sincerely hope for development of a new therapy with less toxicity for relapses of NS. In this report, we demonstrate a case of a 2-year-old boy with frequently relapsing NS, whose frequent relapses were successfully treated with azithromycin. Azithromycin treatment prevented the need for long-term immunosuppressive therapy in this case. Azithromycin can be a new treatment option for relapse of NS, with few adverse effects, in selected cases.

Case report

A 2-year-old boy presented to our hospital with periorbital edema in October 2015. His serum albumin was low (1.1 g/dL) and large amounts of protein were detected in the urine (urine protein: 1159 mg/dL, urine creatinine: 84 mg/dL, dipstick test: 4+). There was no suggestion of urinary tract infection (no leukocytes in urine). He was diagnosed with idiopathic NS, initially treated with oral prednisolone. He achieved remission at Day 6. At 1 month after discontinuation of initial prednisolone treatment for 2 months, proteins in urine increased again (first relapse, in January 2016, as shown in Figure 1). Since food sensitivity including gluten could be associated with NS in some cases, all kinds of potential allergens were removed from the

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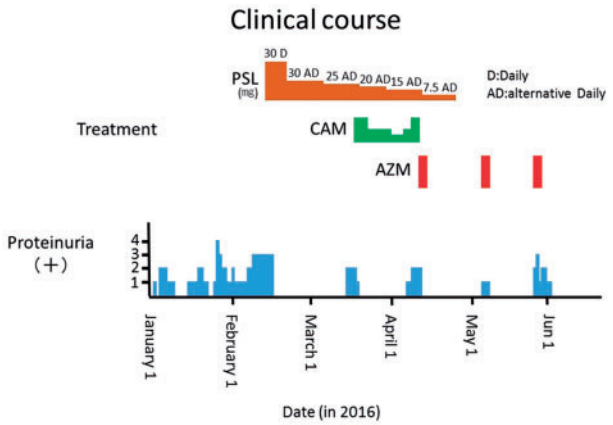

Fig. 1. Clinical course of the patient. Treatment for NS and amounts of protein in urine (dipstick) are shown. Urine dipstick test was performed every day. PSL, prednisolone; AZM, azithromycin; CAM, clarithromycin.

child's diet. However, proteinuria persisted without responding to the dietary restriction. He was treated with oral prednisolone again, and proteins in urine became undetectable in a week. However, as the dose of prednisolone was decreased, proteins in urine increased again. Since several lines of evidences suggest that infection is a trigger and an aggravating factor for NS, clarithromycin in addition with prednisolone was administered to him to treat occult infection. Clarithromycin decreased proteins in urine transiently, however, they increased again in 3 weeks. Immunosuppressive agents were being administered to the patient. Since azithromycin might have some positive effects on NS [1], azithromycin (10 mg/kg, once daily on three consecutive days) was administered instead of clarithromycin to prevent the use of immunosuppressive agents. Soon after azithromycin administration, proteins in urine dramatically decreased and disappeared. Although proteins in urine became positive repeatedly in the next month, repeatedly administered azithromycin suppressed secretion of protein in urine in each time. There were no more relapses until July 2017. Azithromycin prevented the need for long-term immunosuppressive therapy in this case.

Discussion

Azithromycin is an antibiotic with immunomodulatory activities. An additional positive effect of azithromycin on corticosteroid induction therapy in NS was recently reported [1], and this report suggested that azithromycin possibly suppresses disease activity in NS. However, the effect of azithromycin on relapses in NS have not been explored. Here, we demonstrated a significant beneficial effect of azithromycin on frequent relapses of NS. In this case, prednisolone treatment was not effective enough to suppress disease activity and additional azithromycin treatment definitely prevented the need for long-term immunosuppressive therapy. Sole azithromycin treatment also reduced proteinuria in subsequent relapses. Spontaneous remission of NS was not completely excluded, however, proteins in urine repeatedly decreased soon after azithromycin treatment, strongly suggesting that azithromycin has a beneficial effect on NS activity. To the best of our knowledge, this is the first report that demonstrates the possible efficacy of azithromycin on relapse of NS in children. Azithromycin could be a new treatment option for relapse of NS, with few adverse effects, in selected cases.

We cannot elucidate the mechanism of action of azithromycin for NS. However, azithromycin treatment may improve proteinuria in several ways. First, azithromycin may suppress NS activity with its immunomodulative effects [2]. NS is caused by dysregulation of the immune system, and azithromycin may possibly improve imbalance of the immune system. Second, effects of azithromycin on occult infection may be involved in its effect on NS activity. Upper respiratory tract infection is a usual cause of relapse of NS, and azithromycin may suppress bacterial activities, resulting in the improvement of proteinuria. Third, azithromycin may change protein permeability of renal epithelial cells. In bronchial epithelial cells, azithromycin increases the transepithelial electrical resistance of human airway epithelia by changing the processing of tight junction proteins [3]. Azithromycin may have some effects on protein selectivity in renal epithelial cells.

Authors' contributions

H.H. and D.H. conceptualized and designed the study, drafted the initial manuscript and approved the final manuscript as submitted.

Conflict of interest statement

None declared.

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