Minimal Change Nephrotic Syndrome Which Was Most Likely Caused by Chronic Sinusitis

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Abstract

A 33-year-old Japanese man was admitted with severe edema, and a renal biopsy confirmed minimal change nephrotic syndrome (MCNS). CT revealed his severe chronic sinusitis, and he first received antimicrobial therapy, which resulted in decreased proteinuria. The surgical operation for sinusitis resulted in the complete disappearance of proteinuria without corticosteroid or immunosuppressant therapy within one week. MCNS may be triggered by infection, but there are no previously reported cases of MCNS that is completely remitted by infection control alone. Therefore, we herein report the first case of MCNS that attained complete remission following therapy for chronic sinusitis alone, which suggests a strong etiology of chronic sinusitis for MCNS.

Key words: chronic sinusitis, minimal change nephrotic syndrome (MCNS)

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Introduction

Minimal change nephrotic syndrome (MCNS) is a disease encountered by younger generations and has some of the following characteristics: 1) sudden onset of massive proteinuria and severe edema, 2) a good response to corticosteroids, and 3) frequent relapse (1). Its etiology has not yet been fully investigated, although some researchers have hypothesized that the induction of CD80 may occur in podocytes (2). MCNS may be triggered by various stimuli such as infections, drugs and malignancies. Indeed, we have also experienced MCNS cases that are triggered by infection; however, there have been no reports of MCNS case that are completely remitted by infection control alone.

Case Report

A 33-year-old Japanese man had cough for two weeks in the middle of August and was found to exhibit severe edema with proteinuria (4+) at a nearby clinic. Thereafter, he visited Osaka University Hospital and he was immediately admitted to our hospital on the same day (day 1) in September. He was previously diagnosed with nephrotic syndrome at 3 years of age. However, the detailed medical information as to the presence or absence of infection symptoms was not available. A renal biopsy was not performed at this time, but he attained a complete remission with corticosteroid therapy. Since then, the patient had not experienced any relapse for 30 years without any therapy. The laboratory findings on this admission were as follows: serum creatinine (Cr) 0.92 mg/dL, albumin 1.5 g/dL, total protein 4.6 g/dL, total cholesterol 417 mg/dL, C3 190 mg/dL, C4 50 mg/dL, urinary protein (4+), 2.6 g/g Cr and a selectivity index <0.37. The exact value of the selectivity index was not obtained because the urinary IgG was undetectable. A renal biopsy performed on the day of admission (day 1) confirmed MCNS (Fig. 1A), suggesting the use of corticosteroids as first-line therapy. Prior to the planned corticosteroid therapy, the patient underwent a routine examination by an otolaryngolo-
gist to rule out the existence of chronic infection. In the examination, he was suspected of chronic sinusitis and further underwent a CT scan, which revealed that he had severe chronic sinusitis (on day 7; Fig. 1B, C). However, the patient did not exhibit any of the clinical symptoms of sinusitis. The WBC and C-reactive protein (CRP) values were 6,740/μL and 0.19 mg/dL, respectively, which were within the normal ranges. A culture test of the sinus exudate revealed α-Streptococcus sp., coagulase-negative Staphylococcus and Corynebacterium sp. Thus, we first treated with antibiotics from day 8 for 4 weeks. CT (Fig. 1D) on day 28 confirmed the partial amelioration of chronic sinusitis. During the antimicrobial therapy, proteinuria gradually decreased but persisted (Fig. 2). Thus, the patient underwent a surgical operation for chronic sinusitis on day 38. Immediately after the operation, proteinuria was temporarily aggravated; however, 1 week after the operation, his proteinuria dramatically and completely disappeared without steroid or immunosuppressant treatment. A culture test of the sinus exudate at the operation revealed coagulase-negative Staphylococcus and Corynebacterium sp. All of the tested WBC and CRP values were within the normal ranges until the surgical operation and were not associated with the amount of urinary protein.

Discussion

MCNS is a disease of unknown etiology, although some hypotheses have been raised. A sudden onset of massive proteinuria and a dramatic good response to corticosteroid therapy are notable features. MCNS can be triggered by various stimuli such as infections, drugs and malignancies. Corticosteroid therapy has been the first choice for decades. Indeed, MCNS may be triggered by infection; however, there have been no previous reports of MCNS cases that are completely remitted by infection control. Our study is the first to report an MCNS case which attained complete remission by infection control alone. All of the tested WBC and CRP values were within the normal ranges until the surgical operation and were not associated with the amount of urinary protein.

A previous report showed that nephrotic syndrome was ameliorated with a surgical operation for sinusitis (3). In the report, the renal histology was membranous nephropathy; however, complete remission was not attained by the surgical operation for sinusitis, unlike in the present case. In general, MCNS patients attain complete remission within 19 (12-37) days after the initiation of oral corticosteroid therapy (4). However, in the present case, the patient was able to attain remission in 7 days by the surgical operation for sinusitis without any steroid or immunosuppressant treatment.
This dramatic remission and shorter period of time to complete remission strongly suggests that chronic sinusitis is a direct cause of MCNS in our case. It has been previously reported that nephrotic range proteinuria may occur in coagulase-negative Staphylococcus-induced infections in sinusitis with hypocomplementemia (5). In the report, a renal biopsy was not performed; however, the same bacteria may have caused MCNS in the present case without hypocomplementemia. The infection of coagulase-negative Staphylococcus in the upper respiratory tract or head and neck area may be a trigger of nephrotic syndrome, however, Staphylococcus is part of the normal flora in the nasal or paranasal cavity. Furthermore, we did not rule out viral infection in the present case. Thus, we should be cautious about concluding that Staphylococcus is the causative microorganism.

As to the relationship between sinusitis and glomerulonephritis, it has been previously reported that sinusitis often precedes glomerulonephritis in children and, in most of the cases, sinusitis and glomerulonephritis were concurrently cured (6). This observational study in children reinforces the notion that sinusitis can be a cause of glomerulonephritis. In general, the mechanism of MCNS is not precisely known, although it is hypothesized that the induction of CD80 in podocytes is triggered by circulating cytokines, microbial products or allergens and is perpetuated by regulatory T cell dysfunction or impaired autoregulatory podocyte functions (2, 7). However, recent reports or evidence from clinical practice suggest that rituximab, an anti-CD20 monoclonal antibody, ameliorated the refractory nephrotic syndrome, including frequently relapsing MCNS (8, 9). The etiological analysis is difficult because rituximab leads to direct lysis of B cells only, not T cells. Although MCNS is caused by various stimuli or causes, such as viral infection, malignant lymphoma, non-steroidal anti-inflammatory drugs (NSAID) treatment or allergies, a clear distinction of the mechanism based on the stimuli is difficult. In the present case, the causative microorganism responsible for the infection-induced MCNS was difficult to determine. Because the local symptoms, such as headache or nasal obstruction, and the systemic inflammatory laboratory data were all negative, we should consider sinusitis as a focal infection in the head and neck area. Systemic cytokines or lymphokines, such as IL-13, or microbial products derived from sinusitis may have caused the high permeability of the glomeruli. These unknown toxic factors, the production of which would have temporarily increased during the surgical operation by the mechanical stress and would have sharply declined immediately after the surgical operation, may have affected the amount of urinary protein, which peaked a few days after the operation and sharply declined to a negative value one week after the operation. Based on this rapid disappearance of urinary protein after the surgical operation, some of the circulating factors originating from the focal infection site may have caused MCNS, although the precise mechanism is unknown.

In conclusion, our case suggests that MCNS occurs as a result of chronic sinusitis, a kind of chronic infection in the head and neck area. A thorough check-up for chronic infection and aggressive treatment if it exists is necessary for remission, rather than prompt and automatic corticosteroid therapy, in some case of MCNS.

The authors state that they have no Conflict of Interest (COI).

References