Case Report

Dense deposit disease with steroid pulse therapy

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Abstract

Treatment of dense deposit disease（DDD）has not been established yet. Steroid therapy is considered as ineffective for DDD. We report an 8-year-old girl with DDD in whom steroid pulse therapy with subsequent oral steroid therapy led to disease remission. Serum C3 level improved in accordance with the amelioration of clinical signs. This case suggests that steroid pulse therapy with subsequent oral steroid therapy would be effective for some cases of DDD.

（Key words: C3, Dense deposit disease, Remission, Steroid pulse therapy）

Background

Treatment of dense deposit disease（DDD）has not been established yet: a half of the patients with DDD result in end-stage renal failure within 10 years after the onset[1]. Steroid therapy is considered as ineffective for DDD. We report an 8-year-old girl with DDD in whom steroid pulse therapy with subsequent oral steroid therapy led to disease remission.

Case

An 8-year-old girl, with no family history of renal disease, referred to us with gross hematuria. Physical examination revealed no edema but hollow cheek. Blood pressure and serum creatinine（sCr）level were in the normal range in her age（110/50 mmHg and 0.37 mg/dl, respectively）, although serum albumin, serum complement component 3（C3）and complement 50% hemolytic titer（CH50）levels had decreased to 3.2 g/dl, 10 mg/dl（normal range: 84-151 mg/dl）and 15.8 U/ml（normal range: 25-48 U/ml）, respectively. Total cholesterol level increased to 262 mg/dl. Serum complement component 4（C4）level was 24 mg/dl（normal range: 17-40 mg/dl）, staying within normal range. Urine protein-creatinine（Cr）ratio was 2.9 g/g・Cr. A renal biopsy revealed diffuse mesangial cell proliferation and mesangial matrix increase with all glomeruli showing double contours in a light microscope（Figure 1A）. There were no cellular or fibrous crescents in glomeruli detected. Immunostaining revealed granular C3c deposits in the mesangial region（Figure 1B）and the glomerular basement membrane, but no IgG, IgA or IgM deposits. Electron microscopy revealed electron-dense deposits in the mesangial region and the lamina densa（Figure 1C）. We diagnosed this condition as idiopathic DDD. We excluded the secondary DDD by following data: antinuclear antibody, hepatitis B surface antigen, hepatitis C virus antibody were

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all negative. There are no established treatments for DDD. Steroid therapy is generally considered as ineffective for DDD. Some studies, however, showed a good response to steroid in patients with DDD who had few adverse prognostic factors clinically and histopathologically such as nephrotic or nephritic condition or cellular and/or fibrous crescent and tubular atrophy[2, 3]. Therefore, we started steroid therapy, after obtaining informed consent from the patient and her parents. The patient received intravenous steroid pulse therapy (methylprednisolone (mPSL) 15 mg/kg/day three times per week: total doses 180 mg/day x 3) with subsequent oral prednisolone therapy (PSL 0.5-1 mg/kg/day) for 26 months. At eight months after the beginning of this steroid therapy, her proteinuria and hematuria disappeared, and serum C3 and CH50 levels increased to 28 mg/dl and 33.1 U/ml, respectively, although serum C3 level never reached normal range. The PSL therapy was terminated at 28 months after the beginning of this therapy, because she kept clinical remission. At 28 months after the PSL termination, she developed proteinuria and hematuria again. Physical examination revealed no edema, normal blood pressure (100/58 mmHg) but hollow cheek. Serum albumin and sCr levels were in normal range (4.0 g/dl and 0.38 mg/dl, respectively). Serum C3 and CH50 levels decreased to 10 mg/dl and 24.6 U/ml, respectively. Urine protein-creatinine (Cr) ratio was 1.6 g/g・Cr. A repeated renal biopsy revealed the same condition as before, showing no further deterioration. We started intravenous steroid pulse therapy (mPSL 500 mg/day three times per week) with subsequent oral prednisolone therapy (PSL 30 mg/day for four days) for three weeks. Following eight weeks of oral PSL therapy, the dosage was maintained on an alternate day basis. At 14 months after the beginning of the second treatment, urine protein-creatinine (Cr) ratio decreased to 0.37 g/g・Cr and hematuria disappeared, and serum C3 and CH50 levels increased to 25 mg/dl and 32.2 U/ml, respectively, although serum C3 level had not reached normal range (Figure 2).

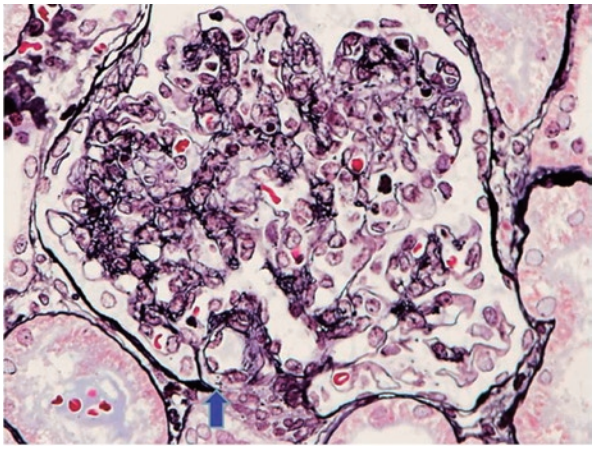

Figure 1A. Initial renal biopsy
Light microscopy revealed diffuse mesangial cell proliferation and mesangial matrix increase in all glomeruli. The arrow indicates a double contour of the glomerular basement membrane (Periodic acid silver-methenamin (PASM)-Masson, ×400).

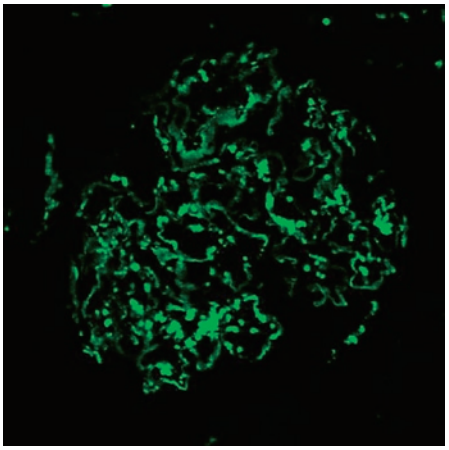

Figure 1B. Initial renal biopsy
Immunofluorescence microscopy revealed granular C3c deposits in the mesangial region.

Discussion

We reported that steroid pulse therapy with subsequent oral steroid therapy was effective for this case with DDD in terms of an anti-proteinuric effect and C3 level improvement.

Treatment of DDD has not been established yet[1]. A randomized control study showed that steroid therapy was ineffective for DDD[4]. However, the present case suggests that steroid pulse therapy with subsequent oral steroid therapy would be effective for some DDD cases. There are some reports that steroid therapy was effective for the cases with DDD when they had no adverse prognostic factors, similar to this case[2, 3].

Although the mechanism of steroid effect for DDD remains unclear, steroid would correct the alternative complement pathway that forms the basic pathophysiology of DDD, considering that serum C3 level increased when proteinuria and hematuria disappeared.

The relationship between serum C3 level and the clinical condition of DDD has not been elucidated[1]. While some studies showed that serum C3 levels were not associated with the clinical condition of DDD[1], others showed that persistent hypocomplementemia was indicative of a poor prognosis[1]. Iitaka et al.[3] reported two cases in whom serum C3 levels were associated with clinical conditions of DDD. These two cases had increased serum C3 level along with the improvement of clinical condition in proteinuria and hematuria, of which course well accorded with that of the present case.

Nasr et al.[5] noted the heterogeneous nature of DDD, both clinically and pathologically. This heterogeneity has led to treatment dilemma. Now, classification based on the disease pathophysiology or clinical course may characterize such subgroups, which may eventually help to identify a subgroup in which steroid therapy may be effective. Thus, classification of DDD into some homogeneous subgroups

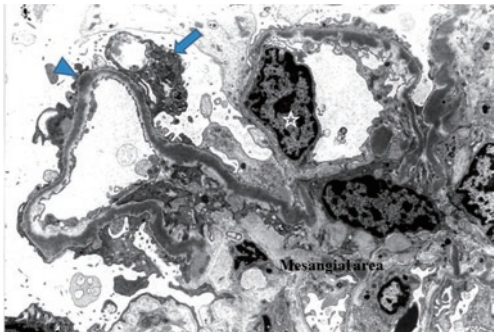

Figure 1C. Initial renal biopsy
Electron microscopy revealed electron-dense deposits in the mesangial region and along the lamina densa of the glomerular basement membrane（×3000）. The arrow and arrowhead indicate the podocyte and electron-dense deposits, respectively. The star indicates the glomerular endothelial cell.

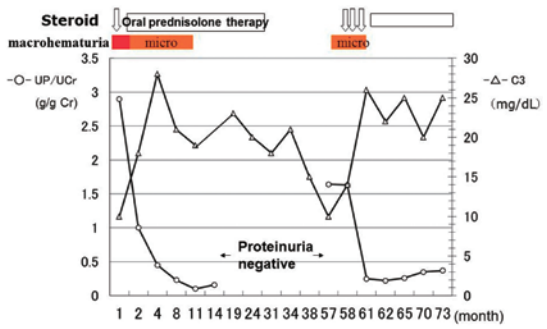

Figure 2. Clinical course
The arrows denote methylprednisolone pulse therapy.
UP/UCr: urine protein/urine creatinine

may help to establish the treatment of this disease.

In conclusion, this case report suggests steroid pulse therapy followed by oral steroid therapy would be considered for the cases with few adverse prognostic factors. Data accumulation is needed for establishing the treatment for DDD.

References

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ステロイドパルス療法で寛解に導入し得た Dense deposit disease の小児例

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要　約

Dense deposit disease（DDD）に対する治療法は確立していない。ステロイド治療は一般にDDD には無効であると報告されている。我々はステロイドパルス療法で寛解し、これに伴い血清 C3値の上昇を示した予後不良因子の少ない DDD の８歳女児例を経験した。予後不良因子の少ない DDD 症例では、ステロイドが有効である可能性がある。

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