A Case of Nephrotic Syndrome with Bilateral Serous Retinal Detachment and Shallow Anterior Chamber Associated with Ciliary Body Edema

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Abstract
Nephrotic syndrome is a disease that causes fluid retention in the body due to loss of protein in the blood, which can lead to serous retinal detachment (SRD) in the macula. We report a case of severe SRD in both eyes and angle closure due to ciliary body edema caused by nephrotic syndrome. A 57-year-old man was admitted to the Department of Nephrology in our hospital for a thorough examination of his generalized edema. He was diagnosed with nephrotic syndrome but proved to be refractory to steroid treatment. Due to distortion symptoms in both eyes on the 30th day of hospitalization, the patient was referred to our department. Best-corrected visual acuity (BCVA) was 0.8 in the right eye and 1.0 in the left eye. Slit lamp examination and anterior segmental optical coherence tomography (OCT) showed shallow anterior chambers in both eyes. Fundus and macular OCT demonstrated severe SRD in the posterior pole of both eyes. After observing the presence of hypoalbuminemia, we considered the possibility of SRD and angle closure due to ciliary edema that resulted from the leaks associated with the nephrotic syndrome. Thereafter, ocular findings improved in conjunction with systemic symptom improvements associated with ultrafiltration and low-density lipoprotein apheresis. On the 60th day of hospitalization, his BCVA improved to 1.2 in both eyes, SRD disappeared, and the anterior chamber depth normalized. This case demonstrates the importance of recognizing SRD and angle closure associated with ciliary body edema as complications linked with nephrotic syndrome.
Purpose

The main symptoms of nephrotic syndrome, which is a renal disease, include severe proteinuria, hypoalbuminemia, edema, and dyslipidemia [1]. There have also been a few reports of serous retinal detachment (SRD) being associated with nephrotic syndrome [2, 3]. The mechanism of SRD is said to involve intratissue fluid retention due to systemic fluid overload and hypoalbuminemia. Uveitis, which is an inflammatory disease, can additionally cause exudative changes, with severe cases potentially leading to secondary angle closure glaucoma. One of the disease mechanisms is associated with ciliary body edema, which has also been reported in Vogt-Koyanagi-Harada disease [4]. Although ciliary body edema is often caused by an exudative mechanism due to inflammation, similar to that found in Vogt-Koyanagi-Harada disease, angle closure can also be caused by leaks associated with noninflammatory diseases, such as nephrotic syndrome. We report a case of severe SRD and angle obstruction due to ciliary body edema in both eyes in conjunction with nephrotic syndrome.

Case Presentation

A 57-year-old man, with no medical history, no obesity, height of 173 cm, and weight of 65.4 kg, visited the Department of Nephrology in our hospital with a chief complaint of generalized edema that had progressed over several days. Blood pressure was 120/80 mm Hg at the time of his first visit, with a reported increase in his weight from 65.4 kg to 78.3 kg. Urine protein was 14.5 g/gCr. Blood tests showed that the total protein was 4.2 g/dL, albumin (ALB) 1.2 g/dL, and low-density lipoprotein (LDL) cholesterol was elevated at 295 mg/dL. As nephrotic syndrome was suspected, the patient was admitted to the hospital the next day. A thorough examination determined there was no evidence of secondary nephrotic syndrome, such as amyloidosis, or collagen diseases, such as systemic lupus erythematosus (SLE) and vasculitis syndrome, or any diabetic nephropathy. The patient was referred to our department on the second day of admission for a fundus examination. Initial examination findings showed that best-corrected visual acuity (BCVA) was good in both eyes (1.2), and spherical power was −1.75 D in the right eye and −1.50 D in the left eye, indicating mild myopia. There were no abnormal findings in the anterior segment, intermediate segment, or fundus.

Minimal change nephrotic syndrome was suspected due to the high selectivity of urine protein and the absence of specific changes observed in the renal biopsy. Although the patient was treated with two courses of steroid pulse therapy (methylprednisolone 500 mg for 3 days) and given prednisolone 40 mg post-treatment, there was little improvement. Due to the steroid-resistant nephrotic syndrome, cyclosporine medication was started. Edoxaban tosylate hydrate was also used to prevent thrombus formation. However, even after 1 month of hospitalization, the response to the treatment was poor, with no significant improvement of the serum ALB level beyond 1.6 mg/dL. In addition, his weight increased to 69.8 kg and pleural effusion was observed. Furthermore, renal function worsened, with a creatinine (Cre) of 4.30 mg/dL and blood urea nitrogen (BUN) of 123 mg/dL. The blood pressure was 169/103 mm Hg, which was elevated as compared to at the time of admission. As the patient began to have distorted vision in both eyes at this time, he was referred to our department again, which was within 35 days after his original admission.

Upon re-examination, BCVA had decreased to 0.8 in the right eye and 1.0 in the left eye. Spherical power was −3.25 D in the right eye and −2.75 D in the left eye, indicating an increase in the myopia. There was no increase in the intraocular pressure, with 16 mm Hg in the right eye and 15 mm Hg in the left eye. The anterior segment findings demonstrated there was mild conjunctival edema in both eyes (Fig. 1a, b). Although both eyes had shallow anterior chambers,
there was no intra-anterior chamber inflammation observed. Optical coherence tomography (OCT) of the anterior segment showed enlargement of the ciliary body and choroidal dissection in both eyes (Fig. 1c,d), with an anterior chamber depth (ACD) of 1.894 mm in the right eye.
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and 1.904 mm in the left eye, which indicated a shallow anterior chamber. Fundus findings in both eyes showed SRD with extensive macular edema observed in about 4 papillae in the posterior pole (Fig. 1e, f), without any noted inflammation or hemorrhage. Macular OCT showed bilateral high SRD with intraretinal edema (Fig. 1g, h). As we found the hypalbuminemia was related to the nephrotic syndrome, this suggested the possibility that the SRD was associated with the increased interstitial fluid that was related to the observed fluid leakage from the vessels to the interstitium.

Hemodialysis (ultrafiltration + LDL apheresis) was started in the Department of Nephrology at 36 days after admission. There was a gradual correction of the hypoalbuminemia, reduction of edema, and weight loss observed, with improvement of the distortional vision symptoms accordingly. After 45 days of hospitalization, the patient’s weight was reduced to 75.9 kg, and there was improvement of his renal function, with a Cre of 1.61 mg/dL and a BUN of 24 mg/dL. In conjunction with the improvement of his general condition, a subsequent anterior segmental OCT demonstrated there was disappearance of the ciliary body-choroidal dissection, along with enlargement of the ACD to 2.275 mm in the right eye and 2.254 mm in the left eye. After 60 days of hospitalization, the ACD opened to 2.604 mm in the right eye and 2.655 mm in the left eye, in conjunction with improvement of the angle obstruction (Fig. 2c, d). Simultaneously, the SRD in the posterior pole almost completely disappeared (Fig. 3e, f).

In addition, the macular OCT showed that the macular edema and SRD disappeared, although the mild outer layer irregularities remained (Fig. 3g, h). Improvement in the nephrotic syndrome was also observed, with the generalized edema disappearing and the patient’s weight improving to 64.1 kg. Blood tests showed an improved ALB of 3.7 g/dL, Cre of 1.28 mg/dL, and BUN of 20 mg/dL, with an almost normalized renal function. The patient was discharged after 70 days of hospitalization.

Fig. 2. Anterior segmental OCT findings on day 45 (a: right eye, b: left eye) and day 60 of hospitalization (c: right eye, d: left eye). After 45 days of hospitalization, there was improvement of the ciliary body-choroidal detachment (a, b: arrows), along with enlargement of the ACD to 2.275 mm in the right eye and 2.254 mm in the left eye. After 60 days of hospitalization, the ACD opened to 2.604 mm in the right eye and 2.655 mm in the left eye, in conjunction with improvement of the angle obstruction (c, d: arrows).
Discussion

Although Izeedini et al. [2] and Blige et al. [3] have reported on cases of SRD that were associated with nephrotic syndrome, these patients only exhibited SRD around the central fovea. Thus, our present case is unique in that the SRD with intraretinal edema was extensive enough to cover the entire posterior pole. Furthermore, this was also accompanied by ciliary edema. While a few cases of choroidal effusion and secondary angle closure glaucoma associated with SLE nephropathy have been previously reported [5, 6], we could find no other studies on SRD with secondary angle closure due to nephrotic syndrome without systemic disease. In addition to the renal disease, since it has been previously reported that hypoalbuminemia due to idiopathic protein leak gastroenteropathy was able to cause SRD in both eyes [7], this suggests that severe hypoalbuminemia due to nephrotic syndrome could potentially be the main cause of the condition in our present case.

In nephrotic syndrome, increased glomerular permeability leads to albuminuria and hypoalbuminemia. This results in a decrease of the plasma osmolality, thereby causing an increase in the transcapillary filtration and movement of fluid from the vessels to the interstitium [8]. As this is accompanied by an increase in the choroidal interstitial fluid due to changes in the permeability of choroidal vessels, this leads to leakage into the subretinal space and the formation of SRD. Secondary angle closure was also thought to be caused by fluid leakage into the ciliary body and the choroid due to decreased plasma osmolarity. Thus, as previously reported [9, 10], this resulted in ciliary body edema and ciliary body-choroidal dissection. Subsequently, this can then cause anterior movement of the ciliary processes and iris lens diaphragm in addition to relaxation of the zonule of Zinn and thickening of the lens, which, as previously reported [11], leads to anterior movement of the lens, thereby increasing myopia and the development of angle closure.

In our current case, the cause of the extensive SRD in the posterior pole with intraretinal edema and ciliary edema may have been due to the poor response to the nephrotic syndrome treatment. Usually, nephrotic syndrome with minimal change disease responds well to steroids [12]. As a result, the edema can usually be quickly reduced with concomitant diuretics and supplementary ALB. Although immunosuppressive agents are normally used in refractory cases [12], the use of immunosuppressive agents in our present case did not stabilize the patient’s condition.
While the patient eventually responded to dialysis treatment, during the 1 month leading up to the introduction of dialysis, there was continued active fluid leakage into the interstitium, along with worsening of the systemic interstitial fluid retention, which included edema of the extremities, pleural effusion, and weight gain. These results suggest that leakage into the interstitium will be conspicuous, in conjunction with the occurrence of intravascular dehydration. Furthermore, the appearance and exacerbation of SRD and ciliary edema in the eye were also found to be linked to extravascular leakage. The improvement in the ocular findings that was associated with the improvement of interstitial fluid due to dialysis treatment additionally suggests that there was a strong involvement of a leaky vessel mechanism in the eye.

Henriques et al. [13] similarly reported finding a case of nephrotic syndrome that was diagnosed a month earlier and then treated with steroids, with the patient subsequently unresponsive to the treatment, which led to the same type of ocular symptoms. Moreover, as was found in our present case, this previous patient also had extensive SRD with intraretinal edema in about 4 papillae in the posterior pole. Although there was no improvement noted in the patient after the administration of diuretics, improvement was observed in conjunction with dialysis treatment. In contrast, Izzedine et al. [2] reported that the SRD was localized to the central fossa, although there was no concomitant renal impairment and the patient quickly improved with diuretic treatment. Thus, the persistence of active leakage may be associated with the increased leakage of interstitial fluid into the eye.

In addition to the noted improvement of the SRD, we also found there was improvement of the ciliary body edema, improvement of the secondary angle closure, and reduction of myopia in conjunction with the improvement of the systemic symptoms. A previous study reported finding a case of hypoalbuminemia secondary to nephropathy associated with SLE that resulted in acute angle closure glaucoma with an intraocular pressure of 32 mm Hg in the right eye and 34 mm Hg in the left eye due to ciliary edema [5]. Even though our present case did not exhibit any increases in the intraocular pressure, angle closure with ciliary edema needs to be recognized as a potential complication. In our patient, we were also able to visually evaluate the opening of the anterior chamber and angle closure along with the improvement of the ciliary edema and ciliary body-choroidal dissection when using anterior segmental OCT. However, it should be noted that this was dependent upon the course of treatment. Since the evaluation is noninvasive and the reported findings do not appear to be dependent upon the examiner, utilization of anterior segmental OCT may be useful for both diagnosis and follow-ups.

We evaluated a case of bilateral SRD and shallow anterior chamber that were caused by ciliary edema, which was associated with nephrotic syndrome. In addition to understanding that SRD is a complication of nephrotic syndrome, it is also necessary to recognize the presence of angle closure associated with ciliary body edema. Anterior segmental OCT in the present case was useful in assessing this condition.

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**Statement of Ethics**

This study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the subject for the publication of this case report and the accompanying images. Ethical approval was not required for this study in accordance with the local or national guidelines.
Conflict of Interest Statement

The authors declare that they have no competing interests.

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Author Contributions

Yasuyuki Takai conceptualized the study and collected the data. Toshiro Sakuma evaluated the results and drafted the manuscript. Keitaro Mashimo collected the data and reviewed the data. Kenji Inoue and Nobuyuki Ebihara participated in the design of the study and critically reviewed the results and manuscript. Yasuyuki Takai, Toshiro Sakuma, Keitaro Mashimo, Kenji Inoue, and Nobuyuki Ebihara read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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