Staphylococcal empyema secondary to IgA nephropathy

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Abstract A 27-year-old male patient, applied to the emergency unit with complaints of high fever, nausea, vomiting, and hematuria. In his physical examination, fever was 38 °C with normal findings in all other systems. The laboratory values were as follows: urea 58 mg/dL, creatinine 2.4 mg/dL, white blood cell count 15.9K/ μ L (PNL: 79 %). In his urine analysis; +1 proteinuria and +3 hematuria were detected. Kidney biopsy was performed. Kidney biopsy interpreted in favor of IgA nephropathy. As the patient had tonic-clonic seizures, cranial CT examination was performed. In the cranial CT, there was a subdural effusion in the anterolateral area of the right cerebral hemisphere with the left shift in the midline secondary to the effusion. Empyema fluid, which was drained postoperatively, was cultured. In the direct examination of the empyema fluid, Gram positive cocci and abundant amount of PNLs were observed. There was no growth in the culture. Although the most commonly encountered agents for post-infectious glomerulonephritis are streptococcus infections, it has been reported that glomerulonephritis attacks may be rarely observed due to staphylococcus infections. Proliferative glomerulonephritis cases are rarely encountered conditions characterized by mesangial IgA accumulations secondary to staphylococcus infections.

Keywords Staphylococcal · IgA nephropathy · Empyema

Introduction

Glomerulonephritis is a disease group, which causes transient or permanent damages in kidneys after a series of inflammatory events in glomerular capillaries and interstitium via immune mechanisms. Majority of glomerulonephritis cases have developed as the result of an immune system disorder. It is caused by the inappropriate response of the body against its own antigens or disordered response against a foreign antigen [1].

There are many causes of glomerulonephritis; infections are one of them. Glomerulonephritis may develop as the result of direct infection of renal tissue or as the result of systemic reaction forming immune responses against some infectious diseases. Immune complexes formed as the result of immune responses accumulate in the glomeruli, and they cause damage to the kidney tissue. Thus, proteinuria and hematuria will ensue [2].

Although the most commonly encountered agents for post-infectious glomerulonephritis are streptococcus infections, it has been reported that glomerulonephritis attacks may be rarely observed due to staphylococcus infections. Proliferative glomerulonephritis cases are rarely encountered conditions characterized by mesangial IgA accumulations secondary to staphylococcus infections. It has been first defined by Koyoma et al. [3] in 1995.

In this present paper, it was aimed to present a case, which applied with a glomerulonephritis attack after subdural empyema development.

Case report

A 27-year-old male patient who had no accompanying disease, applied to the emergency unit with complaints of

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Fig. 1 Results of kidney biopsy

high fever, nausea, vomiting, and hematuria to 10 days. He was using cocaine 5 months ago. He was diagnosed with sinusitis 2 days ago and prescribed moxifloxacin. However, the patient took the drug at an inadequate dose for an inadequate duration.

In his physical examination, fever was 38 °C with normal findings in all other systems. The laboratory values were as follows: urea 58 mg/dL, creatinine 2.4 mg/dL, white blood cell count 15.9K/ μ L (PNL: 79 %), C-reactive protein: 5.77 mg/dL (normal range 0–0.8 mg/dL). In the urine analysis; +1 proteinuria and +3 hematuria were detected. After samples for blood and urine cultures were obtained ceftriaxone 1 $\times$ 2 g i.v. was started empirically. The proteinuria was detected as 2 g/day in analysis performed in 24-hour urine collection. Anti-nuclear antibody (ANA), and anti-neutrophil antibody (ANCA) were negative; C3, C4, IgA, IgM, and IgG levels were normal. (IgG 890 mg/L, normal range 751–1,560 mg/L; IgA 388 mg/dL, normal range 85.0–453 mg/dL) ASO values were within normal limits. HBsAg, Anti-HCV, Toxoplasma-specific IgM, Parvovirus IgM, and Anti HIV were all negative. Echocardiography was performed to investigate presence of glomerulonephritis due to infective endocarditis, and no vegetation was diagnosed. In the abdominal ultrasonography, kidney dimensions were bilaterally increased, and they were detected as grade 1–2. Kidney biopsy was performed on the third day of his hospitalization.

The results of immunofluorescent examination of kidney biopsy were fibrinogen (–), IgA (+), IgG (–), IgM (–), C3 (+), C1q (–), kappa (–) and lambda (+). Immunofluorescence microscopy could not differentiate between IgA1 and IgA2.

Histological and histochemical examinations (HE, PAS; MT; MS, Congo red) of the biopsy materials revealed that nearly all 20 glomeruli had increased mesangial matrix, and patchy cellular increases were observed in fewer numbers of glomeruli. Renal biopsy material was examined under direct microscopy and revealed 20 glomeruli, almost

all of which demonstrated mild to moderate increase of the mesangial matrix. Most glomeruli showed rare neutrophil infiltration, whereas only one had fibrinoid necrosis in the capillary lumen. Roughly 5 % of the interstitium demonstrated inflammatory cell infiltration. There was no mesangial staining in the Congo red staining, which was performed twice. Vacuolar changes were observed in tubular epithelium, and interstitial areas and vascular structures were normal. Electron microscopy could not be performed (Fig. 1).

As the patient had tonic–clonic seizures, cranial CT examination was performed. Subdural effusion in the anterolateral area of the right cerebral hemisphere with the left shift in the midline secondary to the effusion was detected. There were also pan-sinusitis in paranasal sinuses and widespread mucosal thickenings. Patient was operated. The antibiotherapy was switched to meropenem 2 $\times$ 1 g +linezolid 2 $\times$ 600 mg. Gram positive cocci and abundant amount of PNLs were observed in the empyema fluid, which was drained postoperatively. Empyema fluid, blood and urine showed no growth on culture. 32 mg/day dexamethasone was administered as anti-edema treatment. After 4 weeks of steroid therapy, steroid dose was tapered and cut off. In the follow up, urea was 30 mg/dL and creatinine was 1.0 mg/dL at the third postoperative week, and proteinuria was regressed to 600 mg/day. After 4 weeks of antibiotic treatment the patient was discharged with an improved condition. One month later proteinuria was regressed to 140 mg/day and hematuria continued.

Discussion

Subdural empyema is the collection of pus between dura and pia-meters, and 35–65 % of it is caused by sinusitis [4]. Subdural empyema is one of the intracranial complications of sinusitis. Intracranial spread of the infection occurred through neighboring from bone lesions like venous thrombophlebitis, trauma, septic erosion or structural disorders [5]. In our case, septal hematoma and perforation were detected in the left side of the septum due to cocaine use in his postoperative nasal examination.

The most commonly encountered cause of subdural empyema is *Staphylococcus aureus* [6]. In our case, there was no growth in the cultures. This might be due to the antibiotic use before application. However, grape like appearance with non-chain forming Gram positive cocci was detected in the direct examination of empyema fluid; the staining indicated that the causative agent was staphylococci.

Proliferative glomerulonephritis, which is developed secondary to staphylococci infections, and characterized by mesangial IgA accumulation, is a rarely encountered

condition. In a study with 86 acute post-infective glomerulonephritis (APEGN) cases, staphylococci presence was confirmed in 23 % of cases [7]. Wehbe et al. [8] reported from their study performed on 46 glomerulonephritis cases related to staphylococci that this type of glomerulonephritis was more commonly encountered in elderly people. Again in the same study, nephrotic proteinuria and microscopic hematuria were detected as 50 and 83 %, respectively. C3 and C4 levels were determined within normal limits in 72 % of patients. It was determined that glomerulonephritis picture was observed after 1–16 weeks of a latent period after the infection in 25 % of cases. That the patient's symptoms started 10 days ago has been added to the text.

Nasr et al. [7] determined glomerular IgA accumulation in 44 % of APEGN cases. They proposed that pathology of glomerulonephritis related to staphylococci resembled more idiopathic IgA glomerulonephritis than the post-streptococcal glomerulonephritis, which was a subtype of post-infectious glomerulonephritis [7]. Diagnosis of IgA nephropathy and glomerulonephritis related to staphylococci are usually confused. Histopathologic examination of kidney biopsies are not only useful for discrimination. Both clinical features and infection status are important to make diagnosis.

Koyoma et al. [3] reported that staphylococcus related glomerulonephritis cases played a role in the pathogenesis of staphylococcal superantigens. Staphylococcal enterotoxins, which have acted like superantigens, have bound to major histocompatibility complex (MHC) class 2 on the antigen presenting cells. The formed enterotoxin/MHC class 2 complex is bound to V β region in T cells. And this bonding results in T cell activation and cytokine secretion. Cytokines cause polyclonal IgA and IgG production in B cells, and these immunoglobulins end up with immune complexes [3].

The pathological finding of vacuolar change in tubular epithels observed in the patient reported here is likely related to acute tubular necrosis (ATN). Conditions with proteinuria may also lead to vacuolar change. In the case of our patient, proteinuria was not severe, and it did not last long enough to cause such an effect. Thus, ATN is more likely to be behind the vacuolar change, which could have been induced by IgA nephropathy. ATN often raises levels of creatinine, and may lead to vacuolar change [9]. As stated, vacuolar changes might be secondary to proteinuria and ATN.

Pre-existent IgA accumulation in this present case might be diagnosed after the development of this type of renal disease. Because there were no previous tests or kidney biopsy results of the patient, we could not explain the condition.

Surgical drainage and antibiotherapy were performed during the treatment of this present case. Although renal functions and proteinuria were recovered after the treatment, hematuria was sustained. After treatment, leukocytosis and CRP levels receded along with proteinuria. The decline in these parameters might be related to proteinuria receding. The fact that proteinuria receded simultaneously with the amelioration of the infection gives rise to the thought that IgA nephropathy occurred secondarily to the infection.

Recovery of renal functions was confirmed by the investigations performed [3, 10]. Steroid use is debatable in treatment of this type of glomerulonephritis cases. We administered dexamethasone to our patient as an anti-edema agent.

In conclusion, although glomerulonephritis attacks are rarely observed due to staphylococcus infections, staphylococcus infections should be considered in the differential diagnosis of glomerulonephritis.

Conflict of interest The authors have declared that no conflict of interest exists.

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