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A Case of Hemodialysis-Associated Anaphylaxis or Anaphylactoid Reaction, Which Responded Successfully to Very Gradual Tapering Dose of Corticosteroid

To the Editor,

An 84 year old male presented with acute kidney injury (AKI) on CKD (creatinine 8.25 mg/dL) and severe hyperkalemia (K 9.2 mEq/L), and was admitted to the Division of Nephrology and Hypertention, St. Marianna University School of Medicine, Kanagawa, Japan. We considered that AKI on CKD was induced by his dehydration.

Following admission, he was started on hemodialysis (HD) for AKI and hyperkalemia. About 10 min after starting HD, the patient started to complain of dyspnea with wheezing heard over his bilateral chest wall. Suspecting an asthma attack, 125 mg of methylprednisolone (mPSL) was intravenously administered, which successfully resolved the symptom without any interruption of HD. Pulse mPSL (125 mg/each pulse) was administered daily for 3 days, and oral prednisolone (PSL) at a dose of 20 mg was administered daily thereafter. When PSL was tapered to 5 mg, he complained of dyspnea with stridor and became hypoxic within 10–20 min after the start of every hemodialysis session. As soon as the hemodialysis session started, his blood pressure went down to 60 mm Hg from 150 mm Hg. He then required oxygen, β adrenergic inhalation, and pre-medication with antihistamine and oral vasopressor (amezinium metilsulfate) at every HD session. His eosinophil counts increased between the start and the end of each HD session (about 3000/ μ L in HD session on the 54th hospital day) but IgE did not. His

signs and symptoms made us suspect hemodialysis-associated anaphylaxis or anaphylactoid reactions (HDAR) (1). He had not taken ACE-inhibitors. We attempted to use different hemodialysis membranes (cellulose triacetate, polysulfone, polysulfone coating Vitamin E, polymethylmethacrylate, polyester polymer alloy, ethylene vinyl alcohol, all of which were sterilized using gamma-irradiated dialyzer), hemodialysis circuits (saline pre-washed circuit and use of non-ethylene oxide gas sterilization circuit) (2), anticoagulants (heparin, low molecular weight heparin, nafamostat mesilate, argatroban) (3), dialysis solutions (disuse of dialysis solution, acetate free biofiltration), searching for the etiology of HDAR, all of which failed to ameliorate the symptoms (Fig. 1). Despite the pretreatment with antihistamines, symptoms did not improve. Shift of renal replacement therapy to peritoneal dialysis was turned down by the patient and kidney transplantation was not an option because of the absence of a donor. At first, steroid therapy was not tried because of the fear of side effects in this elderly patient. Nevertheless, it seemed difficult to continue HD, and on the 73rd hospital day, 20 mg/day of prednisolone (PSL) was retried and anaphylactoid symptoms completely disappeared. Oral prednisolone was tapered gradually from 20 mg/day to 15 mg/day, then to 12.5 mg/day every week. Eosinophil counts increased and HDAR appeared again when the dose of PSL tapered to 12.5 mg/day. We increased dose of PSL from 12.5 mg/day to 15 mg/day. Afterwards, we tapered steroid doses very gradually (1 mg per week) and could maintain remission of HDAR.

We present our experience of a case with HDAR. The exact cause was not identified but responded

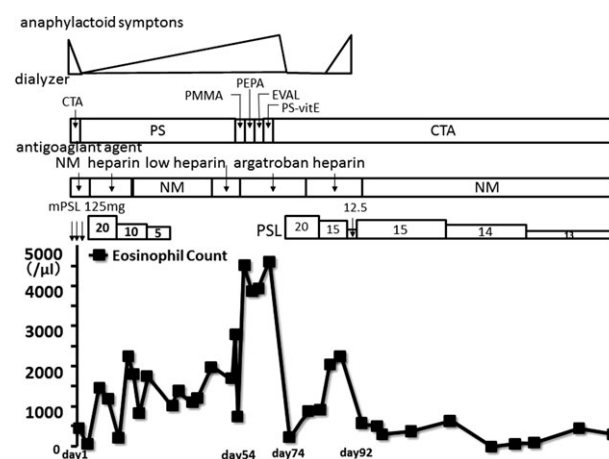


FIG. 1. Clinical course. CTA, cellulose triacetate; PS, polysulfone; PMMA, polymethylmethacrylate; EVAL, ethylene vinyl alcohol; PEPA, polymer alloy; PS-VitE, polysulfone coating vitamin E; NM, nafamostat mesilate.

well to steroid therapy. Even if the cause of severe HDAR is not identified, it is worth while trying steroid therapy when the symptoms are severe. If symptoms or signs of HDAR recur with steroid tapering, the reinstitution of a moderate dose of steroids and slow/gradual steroid tapering therapy should be tried.

Ken Hanada, Sayuri Shirai, Yugo Shibagaki,
and Kenjiro Kimura

*Division Nephrology and Hypertension, Department
of Medicine, St. Marianna University School of
Medicine, Kanagawa, Japan*

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Plasmapheresis-Refractory Thrombotic Microangiopathy in a Hematopoietic Stem Cell Transplant Recipient

To the Editor,

A 54-year-old woman with a history of allogeneic hematopoietic stem cell transplantation (SCT) for acute lymphoblastic leukemia was admitted with generalized malaise and fever of 38.4°C. Her blood pressure on admission was 180/100 mm Hg and she also suffered from chronic renal insufficiency. She was on tacrolimus for cutaneous chronic graft-versus-host disease (GVHD). Results of blood tests on admission are presented in Table 1. Chest X-ray showed a left lower lobe infiltrate, and treatment with antibiotics was commenced. Four days later, she developed several grand mal seizures and hemoptysis. MRI showed focal cerebral edema in frontal and parietal-occipital lobes (Fig. 1). Laboratory tests revealed microangiopathic hemolytic anemia, thrombocytopenia and progressive worsening of renal function (Day 4, Table 1). Cultures of blood, sputum and urine remained sterile. Thrombotic microangiopathy (TMA) was diagnosed and once-daily single plasma exchange (PE) initiated. Tacrolimus was withdrawn and steroid pulse

therapy (500 mg for 3 days) administered. Because of lack of improvement, an intensified twice daily PE was started 3 days later. Due to progressive deterioration of renal function and oliguria, she was started on hemodialysis. After two weeks of treatment, she improved and PE was reduced back to once daily. However, she developed an early exacerbation of her TMA. Twice daily PE regime was reintroduced and a bone marrow biopsy performed. This showed no evidence of recurrence of leukemia. Since our patient did not show any significant improvement we added rituximab at a dose of 375 mg/m² weekly for 4 weeks. After two weeks of concurrent PE and rituximab therapy, her laboratory parameters and clinical symptoms began to improve. Cerebral MRI demonstrated regression of the original lesions, except for a small hemorrhage in the right parietal lobe (Fig. 1). Immunosuppressive therapy for her GVHD was changed to mycophenolate mofetil. She was discharged home and continued hemodialysis as an outpatient. After two months, her renal function has improved and hemodialysis was discontinued. The complex nature of SCT-TMA makes an accurate diagnosis difficult and challenging. SCT-TMA can be attributed to many different causes, such as prior chemotherapy, calcineurin inhibitors, impaired regenerative capacity of the bone marrow, GVHD and infections. There is currently no clear consensus on diagnosis and treatment of SCT-TMA. Slightly different diagnostic criteria for SCT-TMA have been proposed by the Bone Marrow Transplant Clinical Trials Network (1) and the International Working Group (2). Both will require further evaluation and correlation before being adapted into clinical practice. We based our diagnosis of TMA on the presence of microangiopathic hemolytic anemia, thrombocytopenia, renal dysfunction and neurological abnormalities. Though, we are aware that not all patients, particularly with secondary TTP, present with these classical features. It is essential to eliminate all potentially causative factors, particularly calcineurin inhibitors and infections in SCT-TMA. Exclusion of leukemic relapse is of particular importance in patients with poor therapeutic response. Plasma exchange, despite the lack of convincing evidence has been frequently used in SCT-TMA. We started our patient on PE, withdrew tacrolimus and administered steroid pulse therapy. Intensified twice daily PE is typically considered in patients with progressive and refractory disease. This group may also benefit from more intensive immunosuppressive treatment. There is an increasing number of reports on the successful treatment of primary TTP with rituximab. However, only