Dialyzer-related Thrombocytopenia due to a Polysulfone Membrane

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Abstract

A 72-year-old Japanese woman was admitted to our hospital with rapidly progressive glomerulonephritis associated with anti-glomerular basement membrane antibody. Hemodialysis (HD) therapy was initiated on the day of admission using a biocompatible polysulfone (PS) membrane. Her platelet count (PLT; ×10⁴/µL) decreased gradually from 58.7 (day 1) to 5.8 (day 25). Considering the possibility of dialyzer-related thrombocytopenia (DRT), we measured her PLT count before and after the HD session on day 72, which revealed a dramatic decrease of 7.5 to 4.3. This finding suggested that the PS dialyzer caused PLT depletion. After discontinuation of the PS dialyzer, DRT was resolved.

Key words: thrombocytopenia, hemodialysis, polysulfone

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Introduction

Dialyzer-related thrombocytopenia (DRT), which was very common in the era of cellulose dialyzers, is a rare complication of hemodialysis (HD) in the present generation of synthetic polymer dialyzers (1). The most widely used, applied synthetic polymer in Japan is polysulfone (PS), which is used in 50.7% of HD patients and 67.5% of hemodiafiltration patients (2). Although the biocompatibility of PS is generally regarded to be good, there are some reports that suggest a relationship between the use of PS dialyzers and thrombocytopenia (3-5). However, to the best of our knowledge, no report yet exists on PS-related DRT that ensures that non-PS dialyzers do not cause thrombocytopenia. We herein report a case of DRT that was caused by PS membrane usage and not by other membranes, including ethylene vinyl alcohol (EVAL), polyester polymer alloy (PEPA) and polymethyl methacrylate (PMMA).

Case Report

A 72-year-old Japanese woman with kidney dysfunction was admitted to our hospital complaining of general fatigue and gross hematuria that began three weeks previously. Upon a visit to another hospital one week prior to the admission, she was found to be pyrexial and had proteinuria and an elevated serum creatinine (2.0 mg/dL) level. Her serum creatinine level further elevated to 5.8 mg/dL, and she was then referred to our hospital.

On admission, her body temperature was 36.4°C, blood pressure was 146/69 mmHg, and heart rate was 76 beats per minute. A complete blood count demonstrated severe anemia (hemoglobin; 8.0 g/dL), and elevated numbers of white blood cells (11,500/µL) and platelets (PLT; 58.7×10⁴/µL). A biochemical test revealed severe kidney dysfunction (urea nitrogen; 50 mg/dL, creatinine; 7.04 mg/dL), and an immunological test showed elevated levels of C-reactive protein (28.0 mg/dL) and positive anti-glomerular basement membrane (GBM) antibody (>350 U/mL). According to these

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findings, she was diagnosed with rapidly progressive glomerulonephritis associated with anti-GBM antibody. The clinical course after admission is shown in Fig. 1. A flexible double-lumen catheter was inserted into the right internal jugular vein, and HD was performed on the day of admission, and three times a week thereafter. In each HD session, a PS membrane (APS-15SA®, Asahi Kasei Medical, Tokyo, Japan) was used as the dialyzer and nafamostat mesilate (Futhan®, Torii Pharmaceutical, Tokyo, Japan) as the anticoagulant. Steroid therapy (from day 2) and plasma exchange (from days 3 to 17 and days 35 to 46) failed to relieve her kidney dysfunction. A renal biopsy on day 15 revealed irreversible glomerular damage (diffuse glomerular crescent formation, 22 of 25 glomeruli; global sclerosis, 21 of 25 glomeruli; hyalinosis, 1 of 25 glomeruli, and fibrinoid necrosis). Accordingly, the withdrawal of maintenance HD therapy was considered to be difficult, and thus an arteriovenous fistula was made on day 50.

After admission, the PLT count (×10⁴/μL) decreased gradually from 58.7 (day 1) to 5.8 (day 25). No elevation of blood fibrinogen/fibrin degradation products (FDP) or FDP D-Dimer was observed. Heparin-induced thrombocytopenia was excluded, as heparin-PF4 antibody was not detected in her plasma. Discontinuation of drugs suspected to cause thrombocytopenia (rabeprazole and sulfamethoxazole/trimethoprim) had no effect on her PLT count. Leukopenia was not observed, and anemia was properly controlled by an erythropoiesis-stimulating agent.

Considering the possibility of DRT, we measured her PLT count before and after the HD session on day 72. As shown in Fig. 2, her PLT count dramatically decreased from 7.5 to 4.3. Similar decreases were observed after each consecutive HD session in which a PS membrane was used (days 77, 79, 81 and 86). To determine whether such a trend would be

Figure 1. Clinical course after admission. HD: regular hemodialysis, PE: plasma exchange, PSL: prednisolone, mPSL: methyl prednisolone (500 mg/day × three days), FFP: fresh frozen plasma

![Graph showing clinical course after admission](image-url)
Figure 2. Platelet count data for each dialyzer membrane. PS: polysulfone, EVAL: ethylene vinyl alcohol, PEPA: polyester polymer alloy, PMMA: polymethyl methacrylate, Pre: predialytic platelet count, Post: postdialytic platelet count, Post-Pre: the difference between the Pre and Post values

| Dialyzer               | Sterilization technique | Type (dry or wet) | Containing PVP |
|------------------------|-------------------------|-------------------|----------------|
| APS-15SA (polysulfone) | gamma beam              | wet               | (+)            |
| KF-15 (ethylenevinylalcohol) | gamma beam          | wet               | (-)            |
| FDX-210GW (polyester polymer alloy) | gamma beam       | wet               | (+)            |
| NF-1.6H (polymethyl methacrylate) | gamma beam     | wet               | (-)            |

Table. The Dialyzers Used in This Case.

observed in HD sessions using other types of membrane, we performed HD sessions using EVAL (KF-15, Kawasumi Laboratories, Tokyo, Japan), PEPA (FDX-210GW, Nikkiso, Tokyo, Japan) and PMMA (NF-1.6H, Toray Medical, Tokyo, Japan) membranes after obtaining the patient’s consent. As a result, no PLT decrease was observed after any of the HD sessions in which membranes other than PS were used. The details of the dialyzers used for this patient are shown in Table. After discontinuation of the PS dialyzer, thrombocytopenia was resolved. The patient was discharged from our hospital on day 103 and referred to a local outpatient HD clinic.

Discussion

This case report shows significant transient DRT in a patient on dialysis using a biocompatible PS membrane (APS-15SA). Such DRT markedly improved after the dialyzer was switched to other biocompatible non-PS dialyzers (KF-15, FDX-210GW, and NF-1.6H).

The decrease in the PLT count due to contact between the blood and the dialysis membrane has been well recognized since the dawning era of HD therapy. One of the main mechanisms is the activation of complement by PLT, which form white blood clots. It is speculated that such reaction is common in HD sessions with cellulose dialyzers, but rare in sessions using synthetic polymer dialyzers, including the PS dialyzer.

Potential causative factor(s) for DRT other than the dialysis membrane include the method of sterilization [ethylene oxide (6) and electron-beam (7)] and the hydrophilizing agent (polyvinylpyrrolidone; PVP) of the dialysis membrane used (8). However, all dialyzers used in the present case (including APS-15SA) were sterilized using γ-ray, and not only APS-15SA, but also FDX-210GW contained PVP (Table). Therefore, both PVP and the method of sterilization were not considered to be causes of DRT. Although no PS membranes, other than APS-15SA, were used as the dialyzer, the conditions of the patient highly suggest that the PS membrane itself induced thrombocytopenia. Olafiranye et al. reported a case of DRT induced by PS membrane-dialyzer usage, which was resolved after switching to a cellulose tri-
Figure 3. The structural formulas of polysulfone (A), ethylene vinyl alcohol (B), polyester polymer alloy (C), and polymethyl methacrylate (D).

acetate membrane (9).

Fig. 3 shows the structural formulas of PS, EVAL, PEPA and PMMA. Of these, PS and PEPA are rich in hydrophobic benzene rings. Moreover, the number of hydrophilic groups of PS (one sulphonyl group versus four benzene rings) is fewer than that of PEPA (two carbonyl groups versus three benzene rings). Therefore, the relatively hydrophobic nature of the PS membrane might have contributed to the pathophysiology in the present case. In addition, plasma exchange therapy (from days 3 to 17 and days 35 to 46) and frozen plasma administration (from days 51 to 63) might have accelerated DRT via the supplementation of large amounts of complement (Fig. 1) in this case.

In Japan, a cohort study regarding thrombocytopenia following PS membrane usage was reported in 2008 (10) and a case report was published in 2009 (11). Although it is unclear why such cases were reported in Japan earlier than in Western countries (3-5, 8, 9), these findings might be partially explained by the wide use of PS and unpracticed reuse of dialyzers (12) in Japan.

In conclusion, clinicians must recognize that even a biocompatible PS membrane can induce DRT in some cases, and the peridialytic measurement of PLT may contribute to the identification of DRT in such cases.

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

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