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Pathological perspective reveals a novel hemodialyzer reaction: a case report

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Abstract

Background While the appearance of red clots in the dialyzer and the arterial and venous blood tubing lines is a common phenomenon in every hemodialysis unit, the occurrence of recurrent yellowish-white matter formation in the hemodialysis venous blood pot of a patient is rare.

Case presentation We describe a male 69-year-old male with recurrent yellowish-white matter formation in the hemodialysis venous blood pot and red clots in the dialyzer. This was associated with a significant decrease in his red blood cells count. He had no history of thrombus no pro-thrombotic risk factors could be identified. Light microscopic examination of the deposits revealed the presence of large aggregates of neutrophils, large amounts of fibrin. The yellowish-white matter recurred at the next dialysis session. The occurrence of this episode was completely resolved by switching the dialysis filter and could not be avoided by increasing low molecular weight heparin dosage.

Conclusion The yellowish-white matter and clotting within the dialyzer, as well as severe anemia, could be prevented by changing the type of dialyzer. Due to the rarity of this dialyzer reaction, it is important that awareness of this reaction by early identification be undertaken.

Keywords Hemodialysis, Dialyzer clotting, Yellowish-white matter, Dialyzer reaction

Introduction

The dialyzer is composed of many hollow fibers made from a biocompatible membrane across which solutes are cleared through diffusion and convection. In patients with uremia, after the blood is filtered through the hemodialyzer, some toxins can be removed, and the balance of water electrolytes and acid-base can be maintained, so that the function of the kidney is partially replaced, and only a very small amount of blood remains in the extracorporeal circulatory dialyzer and lines at the end of the dialysis treatment. The hemocompatibility of dialyzers for extracorporeal kidney replacement therapy is of importance to minimize harmful reactions between blood constituents and the membrane [1]. Nowadays, dialyzer reactions are hypersensitivity reactions to the membrane itself or the products used to sterilize the membrane. Dialyzer reactions have been characterized as type A or type B. Type A reactions occur early in the treatment, usually within the first 20 to 30 min. They typically occur during the first treatment but can occur after multiple treatments. Signs and symptoms may include pruritus, urticarial, laryngeal edema, bronchospasm,

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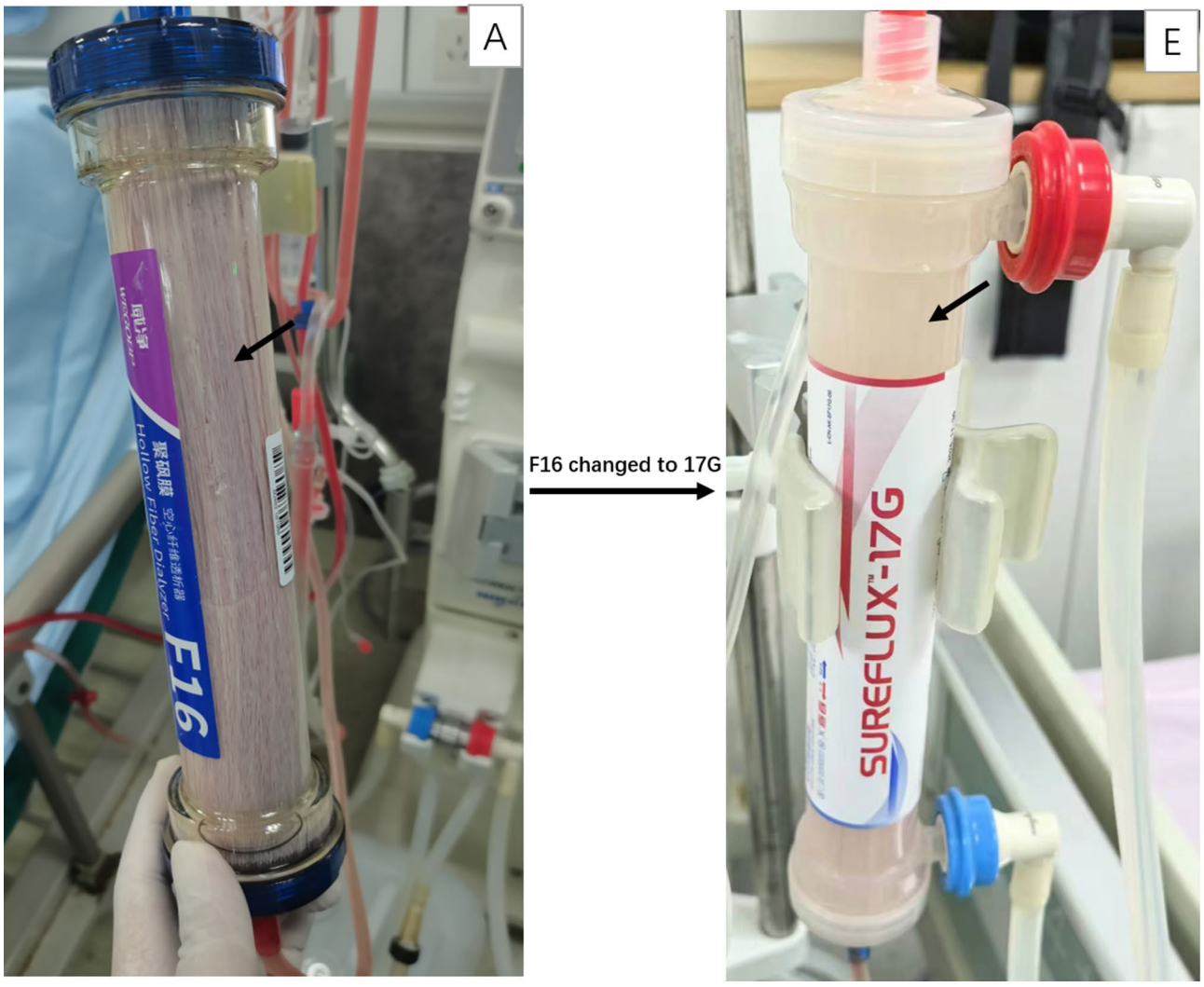

Fig. 1 Clotting was evaluated after hemodialysis with F16 filter (**A**) or with 17G filter (**E**) (black arrows)

dyspnea, chest pain, vomiting, hypoxia, hypotension, and cardiac arrest. Management of a severe reaction includes stopping dialysis without returning blood from the extracorporeal circuit back into the patient. Type B reactions occur later in the treatment and are less severe. Symptoms may include chest and back pain, nausea, and vomiting [2, 3]. In patients who receive hemodialysis, most hypersensitivity reactions to components of the dialysis circuit are due to ethylene oxide or complement activating bio-incompatible membranes [4]. Dialysis is a life-sustaining procedure; therefore, prompt identification and management of the underlying cause of dialysis intolerance are crucial.

We found a novel type of reaction during hemodialysis, which the filter of the venous pot of the extracorporeal circulatory line was repeatedly clogged with a large amount of an unidentified substance and the hemodialyzer repeatedly clotted. Each dialysis was inadequate and extracorporeal blood was repeatedly lost. It was crucial to search for a cause and a solution to the problem of the production of this unidentified substance.

Case presentation

We present the case of a 69-year-old male weighing 62 kg, who was previously diagnosed with type 2 diabetes, diabetic nephropathy, chronic kidney disease stage 5, and uremia. The patient underwent hemodialysis three times weekly with low-molecular-weight heparin anticoagulation (4,000 U per session), utilizing an F16 dialyzer (WEGOBP; Hollow Fiber F16, polysulfone membrane) and an extracorporeal blood circuit for blood purification equipment (WEGOBP, consistent across all patients). Hemodialysis parameters included a blood flow rate of 230–250 mL/min and an average ultrafiltration rate of 400 mL/h. It is worth mentioning that this patient was using an F16 dialyzer for the first 2 weeks. There was no grade 3 coagulation in the dialyzer and no yellow-white deposits in the venous pot. Starting from the third

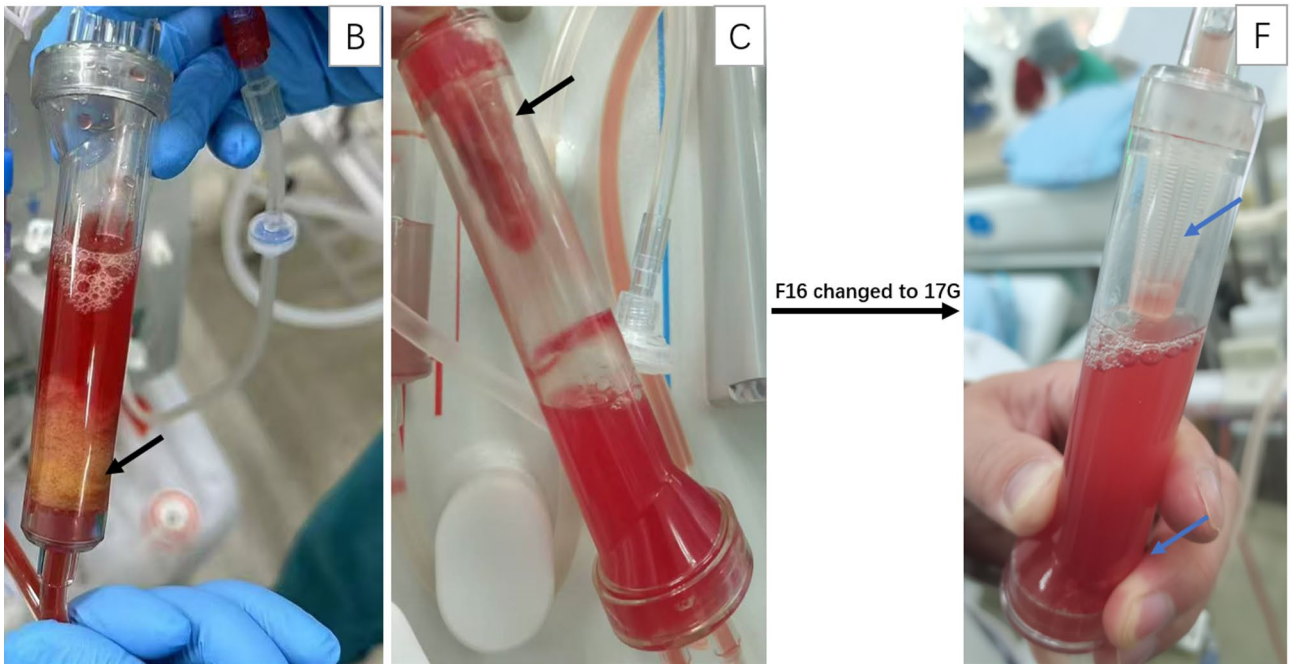

Fig. 2 Yellowish-white matter found adherent to the venous pot after rinse back with F16 dialyzer (black arrows, **B** and **C**) and matter disappeared with 17G (blue arrows, **F**)

week, each dialysis lasted 0.5–1 h and the hemodialysis machine frequently displayed a bubble alarm, accompanied by elevated venous pressure, and the dialysis was terminated prematurely. As a result, the hemodialyzer was observed to be grade 3 clotting (Fig. 1A) and a large amount of yellowish-white unidentified material was visible in the venous pot (Fig. 2B and C), which were deposited or adhered to the pot filters. The patient did not have any uncomfortable symptoms or abnormal signs, such as low blood pressure, rash, and chest tightness. Laboratory measurements are shown in Table 1. The patient's hemoglobin decreased from 90 g/L at the beginning of dialysis to 53 g/L after 3 months of dialysis, which indicated severe anemia. The patient's blood lipids were normal, coagulation indices were normal, the number of leukocytes and the number and ratio of neutrophils and eosinophils in the routine blood work were no obvious abnormalities. Blood biochemistry and clotting function were all within acceptable limits. However, no clinical risk factors could be identified. Thus, the pathologic investigation was performed to elicit the cause of yellowish-white matter in the venous pot.

We fixed the unknown material in the venous pot using 4% formalin and sent it to the Pathology Department. The specimen was subjected to H&E staining (hematoxylin and eosin staining), which revealed abundant neutrophils and erythrocytes, large amounts of fibrin, and scattered individual lymphocyte (Fig. 3D and Fig. S2a). In addition, regarding analysis of blood immune cells, we also conducted immune-histochemical staining, as shown in Fig. S1. CD4 staining is negative. CD8 staining is negative. CD20 staining positive cells are extremely rare. CD68 positive cells are scattered in distribution. Based on the pathological findings, we considered that the patient's blood contact with the membrane surface of the hemodialyzer might have produced a microinflammatory reaction. Then, after replacing the F16 dialyzer with a 17G dialyzer (NIPRO, SUREFLUX-17G, cellulose triacetate membrane), the patient's hemodialysis dialyzer no longer coagulated (Fig. 1E) and the substance in the venous pot also completely disappeared (Fig. 2F). HE staining showed minimal amounts of neutrophils and fibrin (Fig. 3G, Fig. S2b). The patient's hemoglobin level gradually returned to the normal range.

Discussion

Hemodialysis is one of the major life-sustaining treatments for patients with end-stage renal disease. Our patient had been receiving hemodialysis as an outpatient for 2 weeks without any complications. Only during subsequent hemodialysis, he developed repeated episodes of large amount of yellowish-white material in the venous pot within 0.5–1 h of starting the dialysis treatment. Repeated coagulation of the dialyzer seriously affects the quality of dialysis in patients. We were frankly at a loss to explain initially this clinic entity phenomenon.

The dialyzer reactions were clinically classified into type A and type B dialyzer reactions. Most type A reactions have been attributed to ethylene oxide, formaldehyde, and use of ACEIs with acrylonitrile dialyzers, with

Table 1 Relevant laboratory values

Variable	Initiation of dialysis (2 weeks before dialysis)	Recurrent yellowish-white deposits formation in the hemodialysis tubing (3 months after deposits formation)	Disappearance of yellowish-white deposits (2 months after the disappearance of deposits)	Reference range
C-reactive protein, mg/L	13.54	1.85	<0.50	0–10
White blood cell count, x10^9/L	5.96	7.71	5.65	3.5–9.5
Hemoglobin, g/L	90	53	119	130–175
Platelets, x10^9/L	216	411	455	125–350
Neutrophil ratio, %	74	79.6	71.3	40–75
Lymphocyte ratio, %	13.3	8.7	13.1	20–50
Monocyte ratio, %	5.5	5.4	5.3	3–10
Eosinophil ratio, %	5.90	6.00	8.4	0.4-8
Basophil ratio, %	1.30	0.30	1.9	0–1
D-dimer test, mg/L FEU	0.41	-	-	0-0.8
International normalized ratio	1.07	-	-	0.82–1.15
Activated partial thromboplastin time, s	27.6	-	-	22.3–32.5
Fibrin degradation products, mg/L	2.5	-	-	0–5
Triglyceride, mmol/L	1.3	-	-	0.45–1.81
Total cholesterol, mmol/L	2.98	-	-	2.8–5.9
High-density lipoprotein cholesterol, mmol	0.83	-	-	>1.03
Low-density lipoprotein cholesterol, mmol/L	1.78	-	-	<4.10
urea, mmol/L	20.96	17.76	13.26	2.8–7.2
Serum creatinine, umol/L	769	799	718	64–104
Uric acid, umol/L	529	558	377	208.3-428.4
Serum phosphorus, mmol/L	1.68	1.88	1.55	0.81–1.45
Parathyroid hormone, ng/L	261.5	271.5	276.8	15–65
Serum potassium, mmol/L	5.01	3.65	4.47	3.5–5.1
Serum sodium, mmol/L	130.6	140	140	136–146
Serum chloride, mmol/L	101.0	103	104	101–109
Serum calcium, mmol/L	1.90	2.11	1.98	2.2–2.65
Carbon dioxide, mol/L	18.5	21.25	20.12	20–29
Serum albumin, g/L	33.6	37.11	37.87	35–52
Alanine transaminase, U/L	19	7	13	0–50
Aspartate transaminase, U/L	19	10	15	0–50

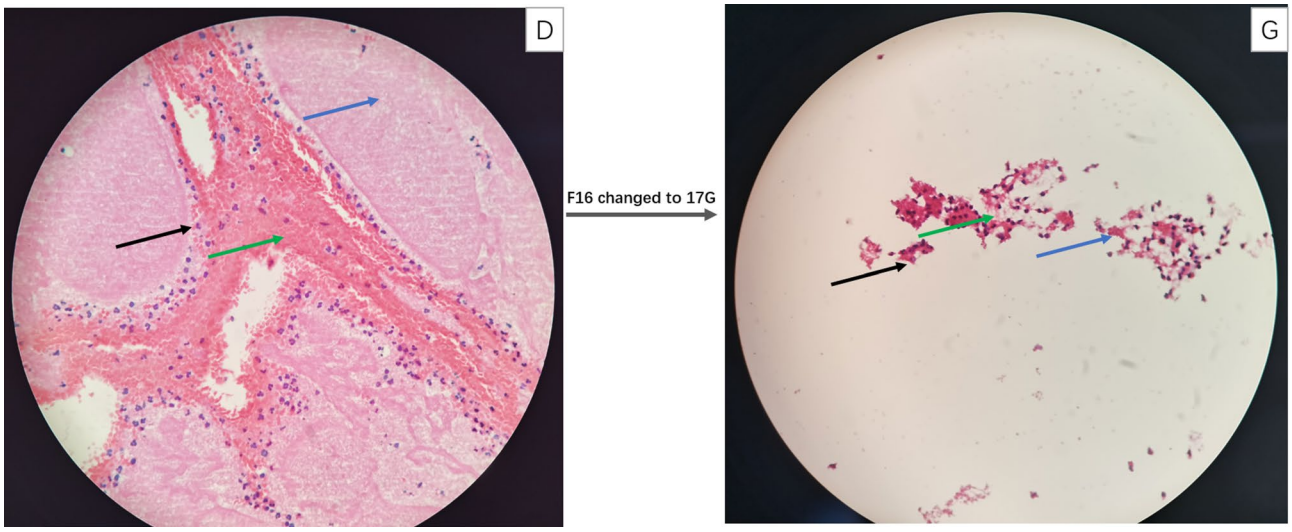

Fig. 3 The light microscopic examination of the yellowish-white deposits in the venous pot with F16 (**D**) or 17G (**G**) showing large aggregates of neutrophils (black arrows) and erythrocytes (green arrows), large amounts of fibrin (blue arrows) (Hematoxylin-eosin stain, x400)

ethylene oxide accounting for most of these reactions. Ethylene oxide and formaldehyde cause a true, immunoglobulin E (IgE)-mediated anaphylaxis production [5]. Cuprophane and polysulfones/polyethersulfones appear to activate complement, which is thought to be the main cause of type B reactions. It was related to free hydroxyl groups on the membrane that activate the alternate complement pathway leading to neutrophil activation and pulmonary leukocyte sequestration. Our patient did not have any clinical symptoms, probably suggesting he had no IgE mediated hypersensitivity allergic response and activated complement pathway. Our patient only showed repeated coagulation of the dialyzer, and yellowish-white material repeatedly appeared in venous pot. This is a new type of dialyzer reaction, that which has not yet been reported yet. We judged this phenomenon by pathological methods as a reaction between the blood and the surface of the dialyzer membrane, which manifested itself as a large number of neutrophils and fibrin aggregation. Therefore, we only changed different types of dialysis membrane materials to solve this phenomenon, which we dialyzed him with a cellulose triacetate membrane based dialyzer and this adverse dialyzer reaction completely resolved. So, this patient should avoid exposure to polysulfone just as anyone allergic to peanuts should avoid any exposure to that antigen. However, the exact mechanism of the reaction between the patient's blood and the dialysis membrane material is unknown and needs to be further studied. Neutrophil aggregation, a critical process in inflammatory responses and immune defense, is regulated by cytokines, chemokines, and intercellular interactions. The mechanism involved include: (1) chemokine- and cytokine-mediated recruitment, where IL-8 (CXCL8) binds to CXCR1/CXCR2 receptors to direct neutrophils to inflammatory sites [6]; TNF-α and IL-1β activate endothelial cells to upregulate adhesion molecules (e.g., ICAM-1, VCAM-1), thereby enhancing neutrophil adhesion and trans-endothelial migration [7]; Neutrophil-derived LTB4 (leukotriene B4) further amplifies aggregation via autocrine positive feedback [8]; (2) adhesion molecule-dependent aggregation, initiated by selectins (P-/E-selectin) mediating neutrophil rolling, followed by integrins (e.g., CD11b/CD18, Mac-1) binding endothelial ICAM-1 to stabilize adhesion and clustering [9, 10]. (3) NETs (neutrophil extracellular traps)-driven positive feedback [11]: Activated neutrophils release DNA protein complexes through NETs, capturing pathogens and activating more neutrophils. NETs components such as histone H3 (H3Cit) and elastase activate endothelial cells and platelets, inducing further secretion of IL-8 and TNF-α to promote neutrophil aggregation. As previously mentioned, the blood cell response is assumed to involve some cytokines and we don't rule out all possible cytokine involvement in the blood circuit. If we observe yellow-white deposits during dialysis in other patient in the future, additional experiments such as cytokine quantification and in vitro modeling will be needed to conduct to further explore the mechanism underlying dialyzer response.

Adverse reactions with biocompatible polisulphone membranes are not frequent [12–14]. MD Arenas et al. described that the severe clinical syndrome of bronchoespasm during hemodialysis with several biocompatible polysulphone membranes made by different manufacturers and with a variety of sterilization methods. On following day he was dialyzed on an celulose triacetate dialyzer and the hemodialysis treatment was uneventful [12]. W H Boer ea al. presented two cases of dialyser reactions, both in patients using a polysulfone. Patient 1 suffered from recurrent attacks of acute dyspnoea, hypoxia and hypotension that occurred early in dialysis sessions, whereas patient 2 presented with unexplained episodes of severe hypotension and vomiting in the initial phases of dialysis [15]. Among 159 patients in our hemodialysis center, only 1 patient was observed to have yellow white substance in venous pot during hemodialysis with a polysulfone membrane. The patient was transitioned to the celulose triacetate membrane dialyzer, which he tolerated well and continued to utilize through the followed hemodialysis course without complication. These cases remind us that "biocompatible" membranes are not free from dialyzer reactions. It also demonstrates a wide range of clinical dialyzer reaction presentations and the complex nature involving a sensitivity reaction to hemodialyzer.

We believe that this is a new type of dialyzer reaction that deserves attention and that pathology plays an important diagnostic role. For clinical cases in which the dialyzer still coagulates or venous pressure is elevated after anticoagulation, rather than simply increasing the anticoagulant and thus the risk of bleeding, this type of novel dialyzer reaction should be taken into consideration. In the future, we believe that improvements in the biocompatibility of dialysis membranes will reduced biological responses elicited by blood-membrane interactions.

Abbreviations

ACEIs	Angiotensin-converting enzyme inhibitors
ICAM-1	Intercellular adhesion molecule-1
VCAM-1	Vascular cell adhesion molecule-1

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12882-025-04180-6.

Supplementary Material 1

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None.

Author contributions
WJL and YPG conceptualized, designed and NSW supervised the study. YCX, TFC, JYY and YJT contributed to the data collection, such as information collection, scanning, and data input and WJL and JF Ganalyzed the data. XIC and YL provided essential images. WJL wrote the manuscript. JHD, YFY supported data collection. All authors reviewed the manuscript.

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Data availability
Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Written informed consent to participate obtained from patient. A copy of the written informed consent is available for review by the Editor of this journal.

Consent for publication
The patient provided written informed consent for the publication of this case report.

Competing interests
The authors declare no competing interests.

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References

1. Wagner S, et al. Hemocompatibility of polysulfone Hemodialyzers - Exploratory studies on impact of treatment modality and dialyzer characteristics. Kidney360. 2020;1:25–35.
2. Greenberg KI, Choi MJ. Hemodialysis emergencies: Core curriculum 2021. Am J Kidney Dis. 2021;77:796–809.
3. Saha M, Allon M. Diagnosis, treatment, and prevention of Hemodialysis emergencies. Clin J Am Soc Nephrol. 2017;12:357–69.
4. Sayeed K, Murdakes C, Spec A, Gashti C. Anaphylactic shock at the beginning of Hemodialysis. Semin Dial. 2016;29:81–4.
5. Kopacz A, Ludwig C, Tarbox M. Atypical cutaneous and musculoskeletal manifestation of SARS-CoV-2: 'COVID-19 toes' and spasticity in a 48-year-old woman. BMJ Case Rep. 2021;14.
6. Carnicelli D, et al. The antibiotic polymyxin B impairs the interactions between Shiga Toxins and Human Neutrophils. J Immunol. 2016;196:1177–85.
7. Ye J, et al. Zebrafish as a model for investigating Klebsiella pneumoniae-driven lung injury and therapeutic targets. Exp Lung Res. 2025;51:11–22.
8. Kawasaki Y, et al. The leukotriene B4 receptor antagonist ONO-4057 inhibits mesangioproliferative changes in anti-Thy-1 nephritis. Nephrol Dial Transpl. 2005;20:2697–703.
9. Kruger P, et al. Neutrophils: Between host defence, immune modulation, and tissue injury. PLoS Pathog. 2015;11:e1004651.
10. Walzog B, et al. A role for beta(2) integrins (CD11/CD18) in the regulation of cytokine gene expression of polymorphonuclear neutrophils during the inflammatory response. FASEB J. 1999;13:1855–65.
11. Wigerblad G, Kaplan MJ. Neutrophil extracellular traps in systemic autoimmune and autoinflammatory diseases. Nat Rev Immunol. 2023;23:274–88.
12. Arenas MD, Gil MT, Carreton MA, Moledous A, Albiach B. [Adverse reactions to polysulphone membrane dialyzers durind hemodialysis]. Nefrologia. 2007;27:638–42.
13. Watnick S, Stooksbury M, Winter R, Riscoe M, Cohen DM. White thrombus formation in blood tubing lines in a chronic Hemodialysis unit. Clin J Am Soc Nephrol. 2008;3:382–6.
14. Sathe KP, et al. Recurrent white thrombi formation in Hemodialysis tubing: A case report. BMC Nephrol. 2015;16:3.
15. Boer WH, Liem Y, de Beus E, Abrahams AC. Acute reactions to polysulfone/polyethersulfone dialysers: literature review and management. Neth J Med. 2017;75:4–13.

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