

Nephrology Case Report: Reaction to Polynephron Based Membrane Dialyzer

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ABSTRACT

Dialyzer-associated reactions, though rare, can significantly impact the quality of life for patients undergoing hemodialysis. This case report presents a 56-year-old male with a history of Glomerulosclerosis and end-stage renal disease (ESRD) on regular hemodialysis, who developed severe coughing and shortness of breathing episodes during the start of dialysis sessions. These symptoms were traced to a specific dialyzer type after the other workup was negative. A switch to a different dialyzer resolved the symptoms, underscoring the importance of considering dialyzer biocompatibility in managing unexplained symptoms during dialysis.

Keywords: dialyzer biocompatibility; hemodialysis adverse reactions; dialysis-associated symptoms.

BACKGROUND

Over the course of haemodialysis history, various types of allergic side effects have been reported during dialysis sessions. While these reactions are not always caused by allergic mechanisms, they result from the interaction between blood and the materials in the extracorporeal blood circuit. These reactions can be seen as a sign of the bio-incompatibility of the materials used¹. Previously, these reactions were categorized as first-use syndrome because they mainly occurred when new dialyzers were used for the first time².

The dialysis membrane in decreasing order of biocompatibility is Synthetic membranes (most biocompatible), Reused cellulose, Cellulosynthetic (Hemophan), Substituted cellulose (cellulose acetate), Cellulose (cuprophane) (least biocompatible)¹.

Patient Details

This case report presents a 56-year-old male with a history of Glomerulosclerosis and end-stage renal disease (ESRD), who developed severe coughing episodes during dialysis sessions.

Medical History

- Long-standing history of Glomerulosclerosis and end-stage renal disease (ESRD).
- On dialysis thrice weekly via right brachiocephalic arteriovenous fistula (BC AVF) for 5 years.
- Past medical history includes hepatitis C, now resolved with negative HCV RNA PCR (3/10/2024).
- Past surgical history: renal transplant (1999), functional endoscopic sinus surgery (2000), total knee replacement (2003), total hip replacement

(2005), umbilical hernia repair (2020), right BC AVF aneurysm repair and closure (14/10/2024), left internal jugular vein permanent catheter insertion (14/10/2024).

Clinical Presentation

- **First Visit:** 12th October 2024, referred for dialysis and AVF closure.
- **Dialysis History:** The last dialysis was on 10th October 2024 in a different hospital. The first dialysis at Thumbay University Hospital post-AVF aneurysm repair and permanent catheter insertion was on 16th November 2024.

Chief Complaints

- **16th November 2024:** Persistent cough for 2 weeks, no improvement to self-administered ciprofloxacin. Increase in eosinophil count. One study done on the allergy to dialysis materials found that 16 of 106 unselected patients developed mild allergic symptoms after hemodialysis; 10 of these patients also developed eosinophilia³.
- **30th November 2024:** Worsening cough which used to extend post-dialysis period, no fever. Chest examination clear.
- **5th December 2024:** Cough, fever (37.8°C), general body ache for 5 days. On auscultation fine basal crepitations noted in the chest. Lab findings included elevated procalcitonin of 63.45 ng/mL (PCT) and C-reactive protein of 49.3 mg/L (CRP) levels, both of which are critical biomarkers for systemic inflammation or infection, raising initial concerns about a potential infectious process or indicating an inflammatory response.

He was treated with amoxicillin-clavulanic acid. Bacterial infections are considered to be the leading cause of pyrexia in haemodialysis patients. The risk of infection is higher in these patients, especially due to the presence of indwelling central venous catheters. While pyrexial reactions have been linked to mycobacterial contamination of the dialysate in the past, such occurrences are now rare, thanks to routine testing of dialysate water⁴.

- **12th December 2024:** Persistent cough after completing antibiotic course for 7 days. During the initial period of the dialysis session, SpO₂ dropped to 93%, high arterial lumen pressure, and blood flow reduced due to continuous machine alarms.
- **14th December 2024:** Severe cough during dialysis, SPO₂ at 93%, similar symptoms as before. Managed with oxygen and symptomatic care. Cardiologist and pulmonologist consultations revealed no significant underlying cardiac or pulmonary pathology.

TABLE 1: Patient laboratory results overview.

Labs	Hb g/dL	Plt x10 ³ /uL	WBC 10 ³ /uL	Eosinophil %	CRP mg/L	PCT
12th October	12.0	-	4.6	2.6	-	-
16th November	11.2↓	74	5.6↓	39.5↑	26.6	-
3rd December	9.7↓	55↓	2.3↓	30.3↓	71.1↑	-
5th December	9.5↓	56↑	3.0↓	53.2↑	49.3↓	63.45
10th December	-	-	-	-	22.4↓	17.76↓
17th December	9.1↓	110↑	10.6↑	56.0↑	16.8↓	115.74↑
19th December	-	-	-	-	-	75.81↓
24th December	-	-	-	-	-	8.90↓
1st January	8.1↓	76↓	5.3↓	49	-	1.75↓
24th January	8.9↑	74↓	3.5↓	14.2↓	-	0.42↓

Intervention

The patient exhibited significant elevations in procalcitonin (PCT) and C-reactive protein (CRP), biomarkers that are typically associated with systemic inflammation or infection. This initially raised concerns about an infectious etiology, but the pattern of symptoms being directly linked to during dialysis sessions pointed towards a dialyzer-related hypersensitivity reaction as a potential cause. (coughing episodes correlating with dialysis sessions). Based on this, a decision was made to change the dialyzer type. Was used Single-use (we do not reuse dialyzer in our center), high-flux dialyzer with a polypropylene housing and polyethersulfone membrane. (Nipro ELISIO™-H Dialyzer). Changed to The Filtryzer NF-H which is a high flux polymethylmethacrylate (PMMA) membrane (Toray Filtryzer NF-H). The patient is doing well on this dialyzer. Post-dialyzer change, seven consecutive dialysis sessions were completed without any adverse events. It also correlated with a drop in eosinophil count and procalcitonin, CRP levels.

Outcomes

The patient reported significant improvement in symptoms with no further episodes of cough or dyspnea. Following the intervention, inflammatory markers showed improvement, with both CRP and

PCT levels decrease, aligning with the resolution of symptoms. The patient remained stable, adhering to the dialysis schedule of three times per week and maintenance medications.

DISCUSSION

The symptoms considering the reaction to dialysis can present in varying frequencies, with the most common being dyspnoea, hypotension, bronchospasm, cough, vomiting, and other gastrointestinal issues. Less frequent symptoms include chest pain, pruritus, urticaria, fever, headache, and confusion. In the most severe instances, there have been reports of cardio-respiratory arrest and death⁵.

The pathophysiology of individual reactions is challenging to explain, as various molecules may trigger different reactions by activating distinct mediators. Consequently, the timing of onset, symptoms, and severity can vary widely. A common factor, however, is that symptoms generally resolve after switching to a new synthetic membrane, most often a cellulose membrane. There have also been reports of symptom resolution when the membrane is replaced with another synthetic type that lacks polyvinylpyrrolidone (PVP) or bisphenol A (BPA), or when similar membranes are used but produced via a different manufacturing process⁶.

There are two types⁷. Reactions that occur during haemodialysis (HD) are the result of an immunoallergic response triggered by the patient's exposure to foreign substances in the extracorporeal circuit and/or the interaction of blood with the dialysis membrane.

Type A: These reactions typically occur within the first few minutes of dialysis, although they can happen up to 30 minutes after dialysis begins. Symptoms include urticaria, coughing, rhinorrhoea, lacrimation, abdominal cramps, pruritus, a burning sensation, angioedema, dyspnoea, and, in severe cases, circulatory collapse or death. These are serious reactions that necessitate the immediate cessation of dialysis, and it is recommended that blood from the extracorporeal circuit not be returned to the patient. Type A reactions can be further categorized into anaphylactic, when mediated by IgE, or anaphylactoid, when they are not mediated by IgE.

Type B: These reactions are more common and generally less severe than Type A. Symptoms include chest pain, dyspnoea, nausea, vomiting, and hypotension. They usually appear 15 to 30 minutes after dialysis starts but can occur later as well. These reactions typically resolve during the session without the need to disconnect the patient. They are thought to be caused by pulmonary leukostasis, which results from complement activation by the dialysis membrane, leading to the generation of C3a and C5a².

The timing of the reaction's onset is highly variable, occurring anywhere from 5 minutes after the start of dialysis to up to one hour before the session ends⁸. This case highlights a rare instance of dialyzer-associated coughing episodes, a condition that can significantly impact the quality of life and compliance in dialysis patients. The prompt identification and change of the dialyzer resolved the symptoms, underscoring the importance of considering dialyzer biocompatibility in patients presenting with atypical symptoms during dialysis. Collaboration between nephrologists, pulmonologists, and cardiologists was crucial in excluding other potential causes of the elevated inflammatory markers and ensuring comprehensive care. Procalcitonin has become a valuable marker for differentiating bacterial sepsis from other types of infections. However, its levels can also rise in conditions that trigger an increase in cytokines, such as burns, chronic kidney disease, trauma, myocardial infarction, and stroke⁹. This case highlights cytokines storm due to dialyzer hypersensitivity reaction as one of the nonbacterial infectious cause of raised procalcitonin.

CONCLUSION

Effective management of these patients demands a multidisciplinary approach, including quick recognition and treatment by the attending physician, as well as the identification of the causative agent(s) and the subsequent avoidance of the implicated compound(s)¹⁰.

In patients undergoing hemodialysis, dialyzer-related hypersensitivity should be considered when unexplained respiratory symptoms are present during dialysis sessions. Immediate intervention with a dialyzer change can lead to symptomatic relief and prevent further complications, ensuring the continuity of effective dialysis therapy.

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