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Case Series

Acute hypersensitivity reactions during hemodialysis: a case series of end-stage renal disease patients

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ABSTRACT

Hypersensitivity reactions during hemodialysis (HD) are rare but potentially life-threatening events. They are often attributed to dialyzer membranes, sterilization agents, or dialysis solutions. This case series highlights acute hypersensitivity episodes in three HD patients at the same center. This report presents a case series of three patients with end-stage renal disease (ESRD) developed symptoms such as back pain, body pain, and shivering approximately 40-45 minutes into their HD sessions. Rapid intervention with hydrocortisone and pheniramine resolved the symptoms. Following the disinfection of equipment and preparation of fresh bicarbonate solutions, HD was resumed uneventfully. Similar timing and symptomatology in multiple patients suggest potential triggers related to dialysate composition, bacterial endotoxins, or other contaminants. This underscores the need for stringent quality control and monitoring in dialysis facilities. Timely recognition and management of hypersensitivity reactions during HD are crucial for patient safety. Further investigation is warranted to identify specific triggers and implement preventive measures.

Keywords: Hemodialysis, Acute hypersensitivity reaction, End-stage renal disease, Dialysate contamination, Dialyzer membrane

INTRODUCTION

Chronic kidney disease (CKD) is a widespread, irreversible, and progressive disease that affects over 13% of the global population.[1,2] One of the major causes of death worldwide, CKD places a heavy burden on low- and middle-income nations.[3] According to a September 2020 study, 843.6 million people worldwide suffer from CKD, and two recognized, widely used treatments for these patients are hemodiafiltration and HD.[4,5]

Dialysis-associated hypersensitivity events, including anaphylactic and anaphylactoid, are well-known consequences. Medication, cellulose membranes, and equipment sterilized with ethylene oxide (EtO) account for the majority of instances.[6] Acute reactions typically manifest as discomfort, angioedema, flushing, pruritus, and dyspnea. Although they are uncommon, hypersensitivity reactions can present with a variety of symptoms. Although the majority of occurrences are minor, some can be fatal, emphasizing the need of identifying and treating such reactions. Identifying the specific allergen responsible can often be a significant challenge. We present a case series of suspected dialysis induced hypersensitivity reactions that first appeared during continuous renal replacement therapy (CRRT) and recurred with HD.

CASE SERIES

Case 1

A 55-year-old male patient with ESRD secondary to hypertension, diagnosed in year 2020, has been undergoing thrice-weekly HD sessions at our center for the past four years. His medical history is notable for a mitral valve repair performed last year, a past cerebrovascular accident (CVA), and hepatitis C for which he received treatment in the year 2014. His current hepatitis C PCR is negative, and he has no known drug allergies (NKDA).

The patient arrived at the center with a 2 kg weight gain from his dry weight, blood pressure of 163/97 mmHg, and a temperature of 98°F. The session utilized a hollow fiber hemodialyzer LoF1 with a polyethersulfone (PES) membrane, primed with normal saline. Vascular access was achieved via a left brachiocephalic AV fistula, and 5000 IU of heparin was introduced into the extracorporeal circuit. HD was initiated using a Fresenius medical care 4008S machine with an ultrafiltration goal of 2000 mL and a rate of 500 ml/min.

The ultrafiltration goals, blood flow, and dialysate parameters for case 1 are summarized in the Table 1.

Approximately 40 minutes into the HD session, the patient reported acute body and back pain, which escalated rapidly and was accompanied by shivering. HD was immediately paused, and the patient was administered 100 mg of intravenous hydrocortisone and 2 mL of intravenous pheniramine. Within minutes, the patient's condition improved, and his vitals remained stable throughout the episode. Following this event, the HD machine was disinfected using citrosteril liquid, and a fresh bicarbonate solution was prepared. HD was restarted, and the session was completed uneventfully.

Case 2

A 72-year-old male patient with ESRD attributed to diabetic nephropathy, presented to the center for his regularly scheduled HD session. His medical history includes hypertension and a prior CVA. He was noted to be stable pre-dialysis, with no weight gain from his dry weight, and his initial vital signs were within normal limits. The hollow fiber hemodialyzer LoF1 with a PES membrane was used, primed with normal saline. Vascular access was through a brachiocephalic AV fistula, and 5000 IU of heparin was introduced into the extracorporeal circuit per protocol.

HD was initiated using a Fresenius medical care 4008S machine with an effective blood flow rate of 295 ml/min and a dialysate flow rate of 500 ml/hr.

After approximately 40-45 minutes of HD, the patient reported body pain and shivering. Although he exhibited no respiratory distress, HD was paused, and intravenous Hydrocortisone 100 mg and Pheniramine 2 mg were administered. The patient's symptoms improved quickly, with stable hemodynamics throughout the episode. The HD machine was disinfected using Citrosteril liquid, and a new bicarbonate solution was prepared. HD was restarted, and the remainder of the session was completed uneventfully.

Case 3

A 30-year-old female patient with ESRD and a history of hypertension presented for her scheduled HD session on the same day as the previous two patients. She arrived with a weight gain of 3.8 kg from her dry weight and was vitally stable at baseline.

A hollow fiber hemodialyzer LoF1 with a PES membrane was utilized, primed with normal saline, and 5000 IU of heparin was introduced into the extracorporeal circuit. HD was initiated using a Fresenius medical care 4008S machine with an ultrafiltration goal of 3800 mL and a rate of 836 ml/min. The ultrafiltration goals, blood flow, and dialysate parameters for case 3 are summarized in Table 1.

Approximately 40-45 minutes into the session, the patient began to experience severe back pain that quickly progressed to generalized body pain, accompanied by shivering and agitation. Recognizing the simultaneous onset of similar symptoms in multiple patients, HD was immediately stopped for all affected individuals. The patient was administered 100 mg of intravenous hydrocortisone and 2 mg of intravenous pheniramine, resulting in prompt recovery.

After the episode, HD machines were disinfected with citrosteril liquid, and new bicarbonate solutions were prepared. HD was subsequently resumed for each patient, with all sessions completed uneventfully.

Table 1: Dialysis parameters for case 1-3.

Parameters	Case 1	Case 2	Case 3
Ultrafiltration goal (ml)	2000	N/A	3800
Ultrafiltration rate (ml/min)	500	N/A	836
Effective blood flow (ml/min)	280	295	295
Dialysate flow (ml/hr)	500	500	500

Table 2: Laboratory findings for case 1-3.

Parameters	Case 1	Case 2	Case 3	Normal values
Gender	Male	Male	Female	
Age (in years)	55	29	70	
Hb (g/dl)	9.0	9.0	10.0	13.5-17.5 (M), 12-16 (F)
MCV (fl)	90.0	81.4	95.9	80-100
Sodium (mmol/l)	147	142	145	135-145
Potassium (mmol/l)	3.5	4.36	3.5	3.5-5.0
Calcium (mmol/l)	6.7	7.9	7.1	8.5-10.5
Urea (mmol/l)	N/A	N/A	175.0	2.5-7.1

DISCUSSION

CKD affects over 50 million people globally and is a growing health challenge. Over 1 million patients rely on HD, which carries risks of complications.[7] One of the potentially fatal side effects of HD is a hypersensitivity reaction to the dialyzer. Dialyzer hypersensitivity reactions have historically been regarded as uncommon occurrences (4 out of 100,000 sessions). However, at the end of the 1980s, Nicholls et al carried out a study in the United Kingdom and highlighted that the problem could be of greater significance.[8,9] A recent study conducted in 2018 in 9 hospitals in Spain showed a total of 37 patients out of 1561 (2.37%) receiving HD had hypersensitivity reactions, highlighting the emerging concern for rising hypersensitivity reactions associated with dialysis.[10]

We describe three cases of early-stage hypersensitivity reactions with symptoms like anxiety, shivering, and body aches. The interim interruption of the session, which was followed by the intravenous infusion of pheniramine and hydrocortisone, was well received. The HD machine had been disinfected and when the session resumed, there had been no recurrence of the hypersensitivity reaction. None of the patients had a history of allergies. The effective response highlights the importance of rapid symptom management, and session resumption under controlled conditions. These interventions proved successful in preventing complications and ensuring continuity of treatment.

Blood-membrane interactions during dialysis trigger hypersensitivity reactions. There are two categories of reactions that have been described: type A and type B.[11] About 4 out of every 100,000 dialysis procedures result in type A responses, which typically happen 30 minutes after the treatment begins.[10] Symptoms range from mild to severe with some cases presenting as anaphylactic shock.[12] Type B reactions have milder symptoms and are mediated by complement activation, typically occur after 30 minutes of dialysis, and are less severe with more biocompatible membranes. Symptoms usually resolve with continued dialysis and supportive care. Reusing dialyzers or switching to biocompatible membranes can help prevent or minimize these reactions.

Dialyzer membranes, made from materials like cellulose, modified cellulose, or synthetic noncellulose (e.g., polysulfone, PAN, AN-69), impact reaction frequency and type. Synthetic membranes are more biocompatible and permeable than cellulose-based ones.[13] In recent years, an increased number of reports focused on hypersensitivity reactions to polysulfone membrane dialyzers.[14] In a case reported by Sánchez-Villanueva et al replacing to cellulose triacetate caused the disappearance of symptoms.[9] Meanwhile, in our case, the HD machine was disinfected with citrosteril liquid, new bicarbonate solutions were prepared and the process was resumed after temporary suspension and completed without any hypersensitivity recurrence.

To increase biocompatibility, the composition of membranes (from cellulose to synthetic membranes), sterilization techniques (removing ethylene oxide), and other components of the dialyzer and tubing (glue, binders, plastics, latex, silicones, etc.) have changed. However, no discernible drop in hypersensitivity reactions has been noted despite this enhanced biocompatibility.[10]

Bigazzi et al explained how pyrogens may back-filter into the blood compartment through high-flux membranes and contaminated fluid, which might result in hypersensitivity reactions in patients receiving dialysis.[15] In case of our patients, all were dialyzed using highly permeable membranes and primed with normal saline, and 5000 IU of heparin was introduced into the extracorporeal circuit.

Dialyzer-related adverse reactions are a significant concern in HD. Nephrologists should remain vigilant, recognizing potential symptoms early based on clinical suspicion. Prompt action and referral to an allergy specialist can help prevent complications and ensure better management of hypersensitivity risks during treatment.

CONCLUSION

Hypersensitivity reactions during HD, though rare, require immediate recognition and management to prevent adverse outcomes. This case series underscores the importance of identifying potential triggers, such as

those linked to dialysate solutions or bacterial endotoxins, and implementing stringent quality control measures. Future research must identify specific risk factors and preventive strategies to enhance patient safety during HD.

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