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Intradialysis cardiorespiratory arrest and anaphylaxis to the dialyzer membrane as a probable etiology in a patient with initiation of renal replacement therapy for chronic kidney disease. Case report.

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Abstract

Introduction: During a dialysis session, hypersensitivity reactions to the dialyzer may occur. Clinically, these conditions can vary in severity, from pruritus, erythema, and facial edema to more severe conditions such as dyspnea, bronchospasm, tachypnea, cyanosis, shock, and cardiac arrest. We present an unusual case of repeated anaphylactic shock, possibly caused by the use of a dialyzer with a helixone membrane.

Clinical case: A 60-year-old hypertensive woman with type 2 diabetes presented with uremia and hypervolemia and underwent dialysis treatment in the hemodialysis program. During the sixth session, she witnessed cardiorespiratory arrest, with recovery of spontaneous circulation after advanced cardiopulmonary resuscitation.

Management: Required management in intensive care with intravenous nitroprusside and intubation with mechanical ventilation.

Evolution: After receiving a new treatment, the patient once again developed hemodynamic instability with hypotension at the beginning of treatment. She was transferred to the peritoneal dialysis program.

Conclusion: An anaphylactic reaction to helixone associated with hypotension and anaphylactic shock is reported.

Keywords:

Cardiac arrest, anaphylaxis, etiology, renal dialysis, case report.

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Hemodialysis is a vital therapy for millions of individuals worldwide. Despite technical and scientific advances, the morbidity and mortality results still need improvement. The hemodialyzer membrane is the primary determinant of the success and quality of therapy. Its properties influence the elimination of solutes and interactions with blood components, defining its biocompatibility. Bioincompatibility may contribute to uremic complications [1]. Developing more biocompatible polymers for use as hemodialyzer membranes is crucial for improving patient clinical outcomes. Various surface-modified membranes have recently been manufactured for hemodialysis to minimize blood incompatibility [2].

The most common acute complications during hemodialysis include cramps (5-20%), nausea and vomiting (5-15%), headache (5%), chest pain (2-5%), and back pain (2-5%). 5%), pruritus (5%), fever, and chills (<1%) [3].

Anaphylactic or anaphylactoid reactions during hemodialysis have been known since 1975. Although numerous articles have been published on this type of reaction, only some cases involving using different membranes, sterilizing agents, medications administered during dialysis, and degrees of water purity, among others, exist. We need well-designed prospective epidemiological studies to determine the exact incidence and extent of these reactions. In a 1985 study, Daugirdas reported 21 severe reactions, including one fatal case, in 260,000 HD sessions. In 1987, the prevalence of 'first use' hypersensitivity reactions in the UK was investigated, and it was found that 1 in 20 to 50 patients were susceptible to an anaphylactoid reaction with a new dialyzer, indicating the magnitude of the problem. [4].

Several types of "allergic" adverse reactions that occur during hemodialysis (HD) sessions have been described throughout the history of hemodialysis. These reactions, which are not always caused by allergic mechanisms, occur due to the interaction of blood with the components of the extracorporeal blood circuit. They can be considered a manifestation of the bioincompatibility of the materials used. Over time, its causes have been identified and, in most cases, corrected.

The first adverse reactions during hemodialysis were described using ethylene oxide as a sterilant for lines and dialyzers. Over time, other disinfection systems, such as water vapor or gamma rays, have replaced ethylene oxide. Early cellulosic membranes, such as Cuprophan membranes, can activate complement and cause hypoxia due to pulmonary leukocyte sequestration. However, these membranes have evolved into asymmetric cellulose triacetate (ATA), eliminating this complication. The combined use of AN69 high-flux membranes and angiotensin-converting enzyme inhibitors (ACE inhibitors) caused adverse reactions associated with increased bradykinins. This problem was solved by modifying the membrane to AN69 [5].

Furthermore, it is essential to remember that adverse reactions may occur associated with the medication administered during dialysis and the contaminants in the dialysis fluid. The epidemiology of these reactions is different and must be carefully considered [6].

Reactions to dialyzer comprise various events that include anaphylactic reactions and other reactions that are not well defined and of unknown etiology.

Dialyzer reactions can be classified as anaphylactic (type A) or nonspecific (type B). Type A reactions manifest clinically in a similar way to anaphylaxis, with symptoms such as dyspnea, a feeling of impending death, and heat in the vascular access or throughout the body. In severe cases, cardiac arrest and even death can occur. Milder patients may present with itching, hives, cough, sneezing, and coryza. Gastrointestinal manifestations such as cramps and diarrhea may also occur. Symptoms usually begin within the first few minutes of dialysis, although sometimes they take up to 30 minutes or more. The safest treatment is to stop dialysis, close the bloodlines, and discard the dialyzer without returning blood to the patient.

On the other hand, symptoms of nonspecific type B reactions include chest pain, sometimes accompanied by back pain. These symptoms usually appear 20-40 minutes after starting dialysis. Treatment in these patients is supportive [7].

Below, a rare clinical case in the hemodialysis service is presented: anaphylaxis as a cause of cardiorespiratory arrest, with a probable etiology of allergic reaction to the dialyzer.

Case

Clinical history

The case of a 60-year-old woman with a personal pathological history of type 2 diabetes mellitus and high blood pressure is presented. In early November 2021, the patient presented with edema in the lower extremities and dyspnea with minor exertion that progressed to dyspnea at rest and orthopnea. He went to a private doctor who requested an analysis, finding a hemoglobin of 9.6 g/dL, urea of 166 mg/dL, and creatinine of 4.9 mg/dL. On November 22, 2021, the patient went to the rural medical center in Azuay (Ecuador), where he was referred to the emergency service of a specialty hospital of the Ecuadorian Social Security Institute in Cuenca, Ecuador.

Physical exam

On admission, physical examination revealed a blood pressure of 155/90 mm/Hg, heart rate of 76 beats/minute, oxygen saturation of 91% with an inspired fraction of oxygen of 21%, and respiratory rate of 19 breaths/minute. In the thorax, rales were found at the bases of both hemithoraxes, and the number of vesicular murmurs decreased at the right base. The heart sounds were rhythmic and synchronous. The abdomen was globulous, soft, and depressible, with air-fluid sounds present. Pitting edema +++ was observed in the extremities.

Driving

The patient was initially assigned to the internal medicine service. On November 24, 2021, a consultation was requested with the nephrology service, where she was diagnosed with stage 5 chronic kidney disease without an urgent need for dialysis. Intravenous diuretic therapy (furosemide) and additional tests were suggested. On November 25, 2021, a consultation with a cardiologist, who reported an electrocardiogram showing left ventricular hypertrophy, was conducted. The same day, the patient was re-evaluated by the nephrology service; a renal ultrasound was reported with echogenic kidneys, and a chest X-ray showed bilateral pleural effusion. Her creatinine level was 5.7 mg/dL, and her urea level was 155 mg/dL. It was decided to place a jugular catheter for hemodialysis.

On November 26, 2021, the patient was transferred to the care of the nephrology service to continue with replacement treatment for kidney function and management of other comorbidities. He received five sessions of hemodialysis, showed improvement, and was discharged to continue with a regular outpatient conventional hemodialysis program.

Evolution

On December 2, 2021, the patient attended her sixth outpatient hemodialysis session. Seven minutes after starting renal replacement therapy, he experienced witnessed cardiorespiratory arrest lasting 8.30 minutes. After advanced CPR, the patient regained spontaneous circulation and was transferred to the intensive care unit. There, she was intubated and connected to mechanical ventilation due to post-cardiac arrest syndrome. Additionally, he was administered nitroprusside to control his resistant high blood pressure. At 24 hours, the patient continued on mechanical ventilation.

On December 4, 2021, the medical team in the intensive care unit decided to continue the patient's hemodialysis. However, 2 minutes into the session, the patient presented with bradycardia and hypotension. Therefore, nitroprusside administration was stopped, and treatment with norepinephrine was started, which improved the patient's symptoms and allowed the completion of the hemodialysis session. The patient remained in the intensive care unit for ten days and received three more sessions of hemodialysis, premedicated with hydrocortisone. Finally, the mechanical ventilation was removed, and the patient was discharged to the nephrology floor.

On December 13, 2021, 24 hours after being discharged from the intensive care unit, the patient experienced a new cardiac arrest 3 minutes into the hemodialysis session. The arrest lasted 4 minutes, and the patient regained spontaneous circulation after receiving advanced cardiopulmonary resuscitation. Due to this event, the hemodialysis session was suspended, and the patient was transferred to the intensive care unit. Based on their medical history, the medical team classified the patient as 4B. Under these conditions, a Tenckhoff catheter was urgently placed on December 14, and peritoneal dialysis was started for three consecutive days without any incident. Finally, the patient was discharged in good condition and is currently on automated peritoneal dialysis. Table 1 shows the patients' initial examinations.

The echocardiogram showed that the cardiac chambers were of average size and that the left ventricle presented discrete concentric hypertrophy. The segmental contractility of the left ventricle was preserved, as was its systolic function, with an ejection fraction of 71%. Left ventricular diastolic function was expected, and right ventricular systolic function was preserved. The mitral and aortic valves did not present morphological or hemodynamic alterations. The tricuspid valve presented discrete functional reflux, and the pulmonary valve did not present hemodynamic alterations. Her pulmonary systolic pressure was 78 mm/Hg, and the IT gradient was 4.1 m/s. The interventricular and interatrial septa were intact, and no thrombi were observed. The pericardium was normal.

The patient was discharged from the continuous outpatient peritoneal dialysis program and continued to visit nephrology outpatient clinics.

Discussion

CKD is commonly treated by dialysis, including hemodialysis (HD) or peritoneal dialysis. These therapies aim to improve patient survival and quality of life. Approximately 3.4 million people worldwide are receiving dialysis, projected to increase to approximately 5 million by 2025. Among the available dialysis modalities, HD is the most widely used [2].

CKD is a frequent cause of consultation with the Nephrology Service in patients hospitalized at the José Carrasco Arteaga Hospital in Cuenca. Many of these patients require the initiation of renal replacement therapy, the modality of which is determined according to clinical severity and socioeconomic situation. In 2020, 30 patients with stage 5 CKD started hemodialysis as the first therapeutic option in this hospital; in 2021, 65 patients were diagnosed. HD is the preferred modality for emergency cases due to the ease of vascular access and the availability of human, technical, and material resources.

In the HD service of José Carrasco Arteaga Hospital, 1,877 procedures were performed in 2020, of which 162 were HD and 1,715 were hemodiafiltration. In 2021, 2,194 procedures were performed, 201 of which were HD and 1,993 hemodiafiltration. High-permeability synthetic helixone membranes are available at the institution.

Despite technological advances in HD, intradialytic complications are not uncommon. The most common acute complications during the HD session in our service, in descending order, are hypotension, vomiting, cramps, chills, high blood pressure, extracorporeal circuit coagulation, and cardiac arrest in isolated patients.

In a review article, Boer et al. described thirty cases of acute reactions to the dialyzer, in addition to two cases reported by the authors. Both patients experienced acute reactions during dialysis with polysulfone dialyzers, presenting symptoms such as dyspnea, hypoxia, and hypotension. However, after switching to cellulose triacetate dialyzers, patients recovered and had no further symptoms [8].

According to the literature, the average age of the patients was 68.7 years (34 to 90 years), and 56.3% were men. In 53.1% of the patients (17 of 32), reactions occurred during the first week after initiating dialyzer exposure. In the remaining 15 patients, the interval between first exposure to the dialyzer and onset of symptoms was considerably longer, with a mean of 11 months (1 to 36 months). In 75% of the patients (24 of 32), reactions occurred within the first 30 minutes of dialysis. In the remaining patients, symptoms manifested between 45 and 120 minutes after the start of dialysis or gradually developed [8].

Table 1. Patient's initial examinations.

Laboratory	Measured Values	Laboratory Reference Values
Hemoglobin	9.4 gr/dl	14-18 gr/dl
Urea	162 mg/dl	10-50 gr/dl
Creatinine	6.1 mg/dl	0.7-1.2 mg/dl
Corrected calcium	8.4 mg/dl	8.3-10 mg/dl
Match	6 mg/dl	
24 hour proteinuria	2340 mg	0 – 140 mg/24 h
Albumin	2.7 gr/dl	3.5-5.5 gr/dl
AST	284	
ALT	183	
HVC, HVB, HIV	Nonreactive	
PTH	173 pg./ml	15-68.3 pg./dl
TSH	5.32	0.4-6 uIU/ml
NT Pro-BNP	14495	
Troponin	578 ng/dl	
C.K.	115 U/L	
CK MB	32 U/L	

The reported clinical manifestations included dyspnea (69%), hypotension (66%), hypoxia (44%), bronchospasm (25%), chest pain (22%), pruritus and urticaria (22%), and abdominal symptoms (22%). %). There were two cases of severe laryngeal edema or stridor. Six cases of cardiorespiratory arrest were recorded (19%), and two patients (6%) died [8].

In our institution, cardiorespiratory arrest occurs in hospitalized patients but not in outpatients who come to the hemodialysis service to continue their treatment.

In a study titled "Incidence of Hypersensitivity during Hemodialysis," 37 (2.37%) of 1561 patients presented with hypersensitivity reactions. Clinical, epidemiological, and analytical information was available for 33 patients (2.11%). The dialysis membranes involved in the responses were polysulfone (23 patients), polynephron (8 patients), polyethersulfone (1 patient), and polyacrylonitrile (1 patient) [9].

Risk factors for sudden cardiac death and cardiac arrest in dialysis patients include coronary artery disease (including acute myocardial infarction), left ventricular hypertrophy, anemia, elevated levels of calcium-phosphorus products, elevated levels of parathyroid hormone (PTH), uremia, chronic fluid overload, inflammation, electrolyte abnormalities, autonomic imbalance (including increased sympathetic tone), heart failure, and left ventricular systolic dysfunction. According to data from the United States Renal Disease Registry System (USRDS), the rate of cardiac arrest increased from 93 events per 1,000 patients two years after initiation of dialysis to 164 events per 1,000 patients five years after onset (1995-1999) [10].

In a retrospective study, approximately 102 cases of cardiac arrest were identified. Ten occurred before dialysis, 72 during treatment, and 20 after treatment. The initial abnormality detected in most cases was ventricular tachycardia or fibrillation [11].

Allergic reactions have been reported for synthetic membranes used in hemodialysis, including polysulfone, polyethersulfone, polynephron, polyarylethersulfone, and polyacrylonitrile [6].

The dialysis membrane is the fundamental component of the dialyzer. Its classification is based on its chemical composition and purification capacity. Membranes are generally polymers composed of repeating identical monomers. According to their composition, they can be divided into cellulose, modified cellulosic cellulose, and synthetic cellulose. However, the current trend is to classify these materials according to their characteristics and properties, such as their degree of biocompatibility, permeability, purifying efficiency, symmetrical or asymmetrical distribution of pores, polarity, and hydrophilic and hydrophobic properties. The most commonly used classification in clinical practice is based on its composition and degree of permeability [12].

Polysulfone membranes are the most commonly used in hemodialysis, but they can cause hypersensitivity reactions or anaphylaxis in some patients. These reactions are associated with polyvinylpyrrolidone (PVP) in the membranes, which modifies their biocompatibility and permeability. The mechanisms involved in these responses can be immunological, dependent on IgE, IgG, complement, or nonimmunological, mediated by direct degranulation of mast cells and basophils. The activation of these cellular mediators produces a variable clinical picture, which can be severe. A membrane component triggers cellular activation in patients who react to synthetic membranes [6].

Dialyzer reactions can be classified as type A or type B. Type A reactions occur early in treatment, usually within the first 20 to 30 minutes. They typically occur during the first treatment but can also happen after multiple sessions. Signs and symptoms include pruritus, cough, urticaria, laryngeal edema, bronchospasm, dyspnea, chest pain, vomiting, hypoxia, hypotension, and cardiac arrest [13].

Type A reactions to the dialyzer are severe and require immediate interruption of dialysis, preventing the return of blood from the extracorporeal circuit. These reactions can be anaphylactic, IgE-mediated, or anaphylactoid, non-IgE-mediated [4].

Management of a severe dialyzer reaction includes stopping dialysis and preventing the return of blood from the extracorporeal circuit. The indicated treatments include the administration of fluids, epinephrine, corticosteroids, and antihistamines [13].

In an acute and severe reaction to the dialyzer, some authors recommend stopping the blood pump, disconnecting the lines, and avoiding blood return to the patient. Symptomatic treatment includes oxygen therapy, intravenous steroids, antihistamines, and bronchodilators as needed. If the patient stabilizes, dialysis can restart with a

different dialyzer. Diagnosis and treatment are based on changing the dialyzer in less severe cases. Currently, there are high-performance dialyzers suitable for online hemodiafiltration [6].

Conclusions

The cardiorespiratory arrest is a severe complication that can occur during a hemodialysis session. For this reason, it is essential that medical and nursing staff constantly monitor patients, and they must be trained to recognize signs of clinical deterioration and act promptly. The immediate treatment of cardiorespiratory arrest is essential for preventing complications and sequelae in patients.

In the present case, proving the etiology is complicated because this is the only type of filter available at the institution. An option to more accurately determine the etiology would be to change the membrane and continue hemodialysis.

Patient perspective

The patient believed that hemodialysis was a risky process due to the shock episodes associated with the start of renal function replacement therapy, and the continuous ambulatory peritoneal dialysis procedure was quickly adopted, which she accepted. Additionally, the patient still lost kidney function.

Abbreviations

HD: hemodialysis.
CKD: chronic kidney failure.

Supplementary information

The supplementary materials have not been provided.

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Does not apply.

Contributions of authors

Jorge Oswaldo Herrera Ordoñez: conceptualization, data curation, formal analysis, research, methodology, and resources.
Oswaldo Mauricio León Cabrera: Conceptualization, Data curation, Formal analysis, Research.
Wilmer Stalin Sanango Reinoso: Conceptualization, Data Curation, Formal Analysis, Research.
Soraya Puertas Azanza: Conceptualization, Data Curation, Formal Analysis, Research.
Carmen Maricela Sevilla Rodríguez: Project administration, Resources, Software, Writing – original draft.

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Availability of data or materials

The datasets generated and analyzed during the current study are not publicly available but can be shared with an academic request.

Statements

Ethics committee approval and consent to participate

Clinical cases are not needed. Consent for participation was obtained from the patient.

Consent for publication

Consent for publication was obtained from the patient.

Conflicts of interest

The authors declare no conflicts of interest.

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References

1. García-Maset R, Bover J, Segura de la Morena J, Goicoechea Diezhandino M, Cebollada Del Hoyo J, Escalada San Martin J, et al. Information and consensus document for the detection and management of chronic kidney disease. Nephrology (Engl Ed). 2022 May-Jun;42(3):233-264. doi: 10.1016/j.nefroe.2022.07.003. Epub 2022 Jul 29. PMID: 36210616.
2. Bonomini M, Piscitani L, Di Liberato L, Sirolli V. Biocompatibility of Surface-Modified Membranes for Chronic Hemodialysis Therapy. Biomedicines. 2022 Apr 3;10(4):844. doi: 10.3390/biomedicines10040844. PMID: 35453594; PMCID: PMC9025662.
3. Jaldo Rodriguez M, Ramón MA. Acute complications during the hemodialysis session. 2023. Nephrology up to date. 03/01/2023. 569
4. Alvarez-de Lara MA, Martín-Malo A. Hypersensitivity reactions to synthetic hemodialysis membranes an emerging issue? Nephrology. 2014 Nov 17;34(6):698-702. English

Spanish. doi: 10.3265/Nefrologia.pre2014.Jul.12682. PMID: 25415569.

5. Tielemans C, Vanherweghem JL, Blumberg A, Cuvelier R, De Fremont JF, Dehout F, et al. ACE inhibitors and anaphylactoid reactions to high-flux membrane dialysis. Lancet. 1991 Feb 9;337(8737):370-1. PMID: 1671272.
6. Pérez García R, Rodríguez Benítez P. Allergic reactions to synthetic membranes in Hemodialysis. 2021. Nephrology up to date. 11/28/2023. 269
7. Salem M, Ivanovich PT, Eng TS, Daugirdas JT. Adverse effects of dialyzers manifest during the dialysis session. Nephrol Dial Transplant. 1994;9 Suppl 2:127-37. PMID: 8065604.
8. Boer WH, Liem Y, de Beus E, Abrahams AC. Acute reactions to polysulfone/polyethersulfone dialyzers: literature review and management. Neth J Med. 2017 Jan;75(1):4-13. PMID: 28124665.
9. Esteras R, Martín-Navarro J, Ledesma G, Fernández-Prado R, Carreño G, Cintra M, Cidraque I, Sanz I, Tarragón B, Alexandru S, Milla M, Astudillo E, Sánchez E, Mas S, Tejeiro RD, Ortiz A, Sánchez R, González-Parra E. Incidence of Hypersensitivity Reactions During Hemodialysis. Kidney Blood Press Res. 2018;43(5):1472-1478. doi: 10.1159/000493662. Epub 2018 Sep 20. PMID: 30235456.
10. Alpert MA. Sudden cardiac arrest and sudden cardiac death on dialysis: Epidemiology, evaluation, treatment, and prevention. Hemodial Int. 2011 Oct;15 Suppl 1:S22-9. doi: 10.1111/j.1542-4758.2011.00598.x. PMID: 22093597.
11. Davis TR, Young BA, Eisenberg MS, Rea TD, Copass MK, Cobb LA. Outcome of cardiac arrests attended by emergency medical services staff at community outpatient dialysis centers. Kidney Int. 2008 Apr;73(8):933-9. doi: 10.1038/sj.ki.5002749. Epub 2008 Jan 2. PMID: 18172435.
12. Huang Z, Gao D, Letteri JJ, Clark WR. Blood-membrane interactions during dialysis. Semin Dial. 2009 Nov-Dec;22(6):623-8. doi: 10.1111/j.1525-139X.2009.00658.x . PMID: 20017832.
13. Greenberg KI, Choi MJ. Hemodialysis Emergencies: Core Curriculum 2021. Am J Kidney Dis. 2021 May;77(5):796-809. doi: 10.1053/j.ajkd.2020.11.024 . Epub 2021 Mar 23. PMID: 33771393.

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