A case of anaphylactoid reaction to acetate in acetate-containing bicarbonate dialysate

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Received: 16 May 2014 / Accepted: 25 August 2014 / Published online: 4 September 2014
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Abstract A 35-year-old man with end-stage kidney disease due to chronic glomerulonephritis was admitted to our hospital to start maintenance hemodialysis (HD). One hour after starting the first session of HD, he experienced general pruritus, urticaria, and dyspnea. Signs and symptoms were resolved by discontinuing HD and administering an antihistamine drug; HD-associated anaphylactoid reactions were therefore suspected. Over the next few HD sessions, we changed the dialysis membrane, anticoagulant, HD circuit and needle, in that order, but general pruritus and urticaria again appeared within 3 h after starting each session of HD. Finally, when we changed the dialysate from acetate-containing bicarbonate dialysate to acetate-free bicarbonate dialysate, urticaria was clearly less than that seen in previous HD sessions, and subsided after discontinuation of HD. Subsequently, 20 mg of oral prednisolone (PSL) was administered 1 h before starting HD, and the patient did not experience general pruritus, urticaria, or dyspnea after starting the session. When administered acetate-containing bicarbonate dialysate after oral PSL pretreatment, the patient again experienced general pruritus, urticaria and dyspnea. Few reports have been published on the occurrence of anaphylactoid reactions during HD using acetate dialysate. We report a rare case of anaphylactoid reactions with acetate in acetate-containing bicarbonate dialysate that were reduced with the use of acetate-free bicarbonate dialysate and oral PSL pretreatment.

Keywords Anaphylactoid reaction · Acetate-containing bicarbonate dialysate · Acetate-free bicarbonate dialysate

Introduction

Anaphylactoid reactions during hemodialysis (HD) are relatively uncommon, but can be life-threatening [1]. The major causes of such reactions are ethylene oxide (ETO), formaldehyde, polyacrylonitrile membranes with or without angiotensin-converting enzyme inhibitors (ACEIs), natural rubber latex (NRL), heparins, and iron [2]. However, very few reports have described the occurrence of anaphylactoid reactions during HD using acetate dialysate [1, 3, 4]. We report a rare case of anaphylactoid reactions induced by acetate-containing bicarbonate dialysate that were reduced by using acetate-free bicarbonate dialysate and oral prednisolone (PSL) pretreatment.

Case report

A 35-year-old man with end-stage kidney disease due to chronic glomerulonephritis was admitted to Seirei Hamamatsu General Hospital (Hamamatsu, Japan) in May 2012, to start maintenance hemodialysis (HD).

He had pollinosis and was allergic to non-steroidal anti-inflammatory drugs, crab, and furred animals (dogs and cats). He sometimes used antihistamines for urticaria.

After admission, maintenance HD was planned to be performed 3 times per week with a polysulfone membrane (PN-100; Nikkiso, Tokyo, Japan) using heparin sodium as an anticoagulant, and acetate-containing bicarbonate dialysate (Table 1).

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Table 1 Dialysis materials and anaphylactoid reactions in each hemodialysis with alternative use of acetate-containing and acetate-free bicarbonate dialysate

Dialyses	1st	2nd	3rd	4th	5th	6th	7th	8th	9th
Dialyser membrane	Polysulfone PN100	PMMA BGL3	Cellulose triacetate FB140	Cellulose triacetate FB140	Cellulose triacetate FB140	Cellulose triacetate FB140	Cellulose triacetate FB140	Cellulose triacetate FB140	Cellulose triacetate FB140
Sterilizer	Autoclave	Gamma ray	Gamma ray	Gamma ray	Gamma ray	Gamma ray	Gamma ray	Gamma ray	Gamma ray
Anticoagulant	Heparin	Parnapararin	Parnapararin	Parnapararin	Parnapararin	Parnapararin	Heparin	Heparin	Heparin
Hemodialysis circuit	Nipro	Nipro	Nipro	Kawasumi	Kawasumi	Kawasumi	Nipro	Nipro	Nipro
Sterilizer	Gamma ray	Gamma ray	Gamma ray	Autoclave	Autoclave	Autoclave	Gamma ray	Gamma ray	Gamma ray
Needle	Covidien	Covidien	Covidien	Medikit	Medikit	Medikit	Covidien	Covidien	Covidien
Sterilizer	Electron beam	Electron beam	Electron beam	Electron beam	Electron beam	Electron beam	Electron beam	Electron beam	Electron beam
Dialysate buffer	Acetate	Acetate	Acetate	Acetate	Acetate-free	Acetate-free	Acetate-free	Acetate	Acetate-free
Pretreatment of antihistamine	Antihistamine	Antihistamine	Antihistamine	Antihistamine	Antihistamine	Antihistamine	Antihistamine	Antihistamine	Antihistamine
Pretreatment of PSL 20 mg	None	None	None	None	None	PSL 20 mg	PSL 20 mg	PSL 20 mg	PSL 20 mg
Anaphylactoid reaction	Positive	Positive	Positive	Positive	Positive (weak)	Negative	Negative	Positive	Negative

One hour after starting the first session of HD, the patient experienced general pruritus, urticaria, and dyspnea. These signs and symptoms subsided after discontinuation of HD and administration of an antihistamine agent and 4 mg of betamethasone sodium phosphate.

Total serum immunoglobulin (IgE) level increased to 837.4 U/ml (normal, <360.9 U/ml), but blood eosinophil level was almost within normal limits (210/ μ l). Signs and symptoms suggested HD-associated anaphylactoid reactions. He had not taken any ACEIs.

Before the second HD session, pretreatment with oral antihistamine had been performed. Three hours after starting the second HD session, pruritus and urticaria appeared again, although the dialysis membrane and anticoagulant were changed to a polymethyl methacrylate (PMMA) membrane (BG-1.3; Toray Medical, Tokyo, Japan) and parnaparin sodium, respectively.

Three hours after starting the third HD session, the same symptoms appeared, even though the hemodialysis membrane had been changed to a cellulose triacetate membrane (FB140; Nipro Pharma, Osaka, Japan).

Next, we changed the sterilization process for the HD circuit from gamma rays (Nipro Pharma) to autoclaving (Kawasumi, Tokyo, Japan), and also changed the needles from sterilization with an electron beam (Covidien Japan, Tokyo, Japan) to a different system also using an electron beam (Medikit, Tokyo, Japan). However, 3 h after starting the fourth HD session, the same symptoms reappeared.

Drug lymphocyte stimulation testing (DLST) against heparin sodium, parnaparin sodium, polysulfone membrane (PN-100; Nikkiso), PMMA membrane (BG-1.3; Toray Medical), and the HD circuits from Nipro Pharma and Kawasumi all showed negative reactions.

Finally, we suspected the dialysate as a cause of anaphylactoid reactions, and changed the dialysate from acetate-containing bicarbonate dialysate (Kindaly AF2; Fuso, Osaka, Japan) to acetate-free bicarbonate dialysate (Carbostar; Ajinomoto, Tokyo, Japan) (Table 2). Three hours after starting the fifth HD session, urticaria was clearly less than that seen in previous HD sessions.

Thereafter, 20 mg of oral PSL was administered 1 h before each session of HD. The patient did not subsequently experience any episodes of general pruritus, urticaria, or dyspnea.

Once we re-challenged acetate-containing bicarbonate dialysate after we got informed consent from patient, because it is important whether he can use acetate-containing bicarbonate dialysate to go hemodialysis clinic. Then he experienced general pruritus, urticaria, and dyspnea again, despite pretreatment with oral PSL. We therefore identified acetate in acetate-containing bicarbonate dialysate as the major cause of his anaphylactoid reactions during HD.

Discussion

The present case demonstrated anaphylactoid reactions induced by acetate in acetate-containing bicarbonate dialysate. Various causes of anaphylactoid reactions during HD have been reported [2], including reaction to the ETO gas used to sterilize dialyzers [5], overproduction of bradykinin under treatment with ACEIs [6, 7], allergy to anticoagulants [8–10], endotoxin contamination of dialysate [11], and bio-incompatibility with the dialysis membrane generating anaphylatoxins such as C₃a and C₅a [12].

We initially suspected dialysis membranes, sterilizing materials, and anticoagulants as the most likely causes of anaphylactoid reactions. However, we could not identify the cause of anaphylactoid reactions among these, despite changing each of the components involved.

Finally, we suspected acetate in acetate-containing bicarbonate dialysate as the cause of the anaphylactoid reactions. In this case, the relationship between anaphylactoid reactions and acetate in acetate-containing bicarbonate dialysate was strongly suggested by the fact that signs and symptoms were apparent both when acetate-containing bicarbonate dialysate was used initially and when the patient was retreated with acetate-containing bicarbonate dialysate.

Use of acetate dialysate has been linked to hypotension, myocardial depression, hypoxia, lipid metabolism abnormality [13], malnutrition [14], and production of inflammatory cytokines [15]. However, anaphylactoid reactions associated with acetate dialysate have been reported in only a very limited number of cases [1, 3, 4]. Ei et al. [3] described a case with hemodialysis-induced asthmatic attacks that subsided soon after acetate-free dialysate was

Table 2 Constituents of acetate-containing and acetate-free bicarbonate dialysate

	Na (mEq/l)	K (mEq/l)	Ca (mEq/l)	Mg (mEq/l)	Cl (mEq/l)	Bicarbon (mEq/l)	Acetate (mEq/l)	Citrate (mEq/l)	Glucose (mg/dl)
Acetate (–) dialysate	140	2.0	3.0	1.0	111	35	–	2	150
Acetate (+) dialysate	140	2.0	3.0	1.0	110	30	8	–	100

used. Caravaca et al. [4] reported a case of hypersensitivity reactions that were attributed to the use of either acetate dialysate or cellulose acetate membrane. Papadakis et al. [1] also reported a case of hypersensitivity reactions that were attributed to the use of acetate dialysate.

Just how acetate dialysate induces anaphylactoid reactions remains unexplained.

In most past case reports, anaphylaxis or anaphylactoid reactions have occurred within minutes after initiation of dialysis. In general, immediate allergy occurs in onset and caused by IgE-mediated activation of mast cells and basophils. However, in our case, anaphylactoid reactions occurred 1–3 h after starting dialysis. We cannot explain why anaphylactoid reactions started after such a long time. We expect another pathway exists and stimulates mast cells and basophils. Further studies are needed to clarify the role of acetate in the development of anaphylactoid reactions linked to HD.

The patient in this case suffered from various allergies, and needed to take oral steroids before dialysis even when acetate-free bicarbonate dialysate was being used. We therefore thought that although the major cause of the anaphylactoid reactions appeared to be acetate, some other factors may have been involved.

Hanada et al. [16] reported a case of hemodialysis-associated anaphylactoid reactions that responded successfully to very gradual tapering of the corticosteroid dose. Our patient also took oral corticosteroids, which proved very effective in reducing anaphylactoid reactions. In this case, attempts will be made to gradually taper oral PSL in the near future.

In summary, we encountered a rare case of anaphylactoid reactions associated with acetate in acetate-containing bicarbonate dialysate. When anaphylactoid reactions are seen with HD, the possibility of acetate-containing bicarbonate dialysate as a cause needs to be taken into consideration.

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

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