Severe cutaneous hypersensitivity to icodextrin in a continuous ambulatory peritoneal dialysis patient

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ABSTRACT: Icodextrin, a glucose polymer, is widely used as an alternative to glucose as the osmotic agent in peritoneal dialysis (PD). We describe a case of a continuous ambulatory peritoneal dialysis patient who developed severe cutaneous hypersensitivity after initiation of icodextrin PD solution. Erythematous skin lesions gradually disappeared after discontinuation of icodextrin PD solution. Although the safety and efficacy of icodextrin PD solution is well documented, clinicians should be mindful of the possibility of severe adverse cutaneous reactions to icodextrin PD solution.

Key words: *Icodextrin, Cutaneous hypersensitivity, Peritoneal dialysis solution*

Introduction

Icodextrin, a starch-derived glucose polymer, has been developed as an alternative to glucose for use as the osmotic agent in peritoneal dialysis (PD) for patients with ultrafiltration failure. Icodextrin PD solution provides a sustained level of ultrafiltration, and its use has been associated with improved fluid management in PD patients. Icodextrin PD solution (Extraneal, Baxter Heathcare) is currently used worldwide and has been available for use in Korea since 2001. It is increasingly used in continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD) patients. It has been shown to be generally safe and tolerable, and has proven itself to be clinically useful in the fluid management of PD patients. However, an approximately 3-fold increase in the risk of developing a new skin rash, when compared with dextrose-based solutions, has been reported, and rare cases of severe cutaneous hypersensitivity have been reported in the literature. We report a case of severe cutaneous hypersensitivity to icodextrin that was resolved with discontinuation of icodextrin PD solution, which is to our knowledge the first report in Korea.

Case report

A 85-year-old woman was admitted to our hospital for severe dyspnea and generalized edema. The patient's past history was unremarkable except for valvular heart disease and hypertension for 20 years for which she did not seek regular medical advice. On admission, she complained of severe shortness of breath, orthopnea, fatigue and generalized edema. Her serum creatinine level on presentation was 6.1 mg/dL; her previous serum creatinine 1 month earlier at another hospital had been 2.6 mg/dL.

On physical examination, the patient's blood pressure was 118/40 mm Hg, heart rate was 90 beats/min, respiratory rate was 25 breaths/min, and she was afebrile. Cardiovascular examination showed a paroxysmal atrial tachycardia on electrocardiogram and her chest x-ray showed significant cardiomegaly and pulmonary edema. The echocardiography showed pseudonormalization of left ventricular filling, grade 4 mitral regurgitation, grade 3 aortic regurgitation and grade 2 tricuspid regurgitation. Ejection fraction was 80%. She was diagnosed as suffering from diastolic heart failure with valvular heart disease and chronic renal failure. She was initially treated conservatively

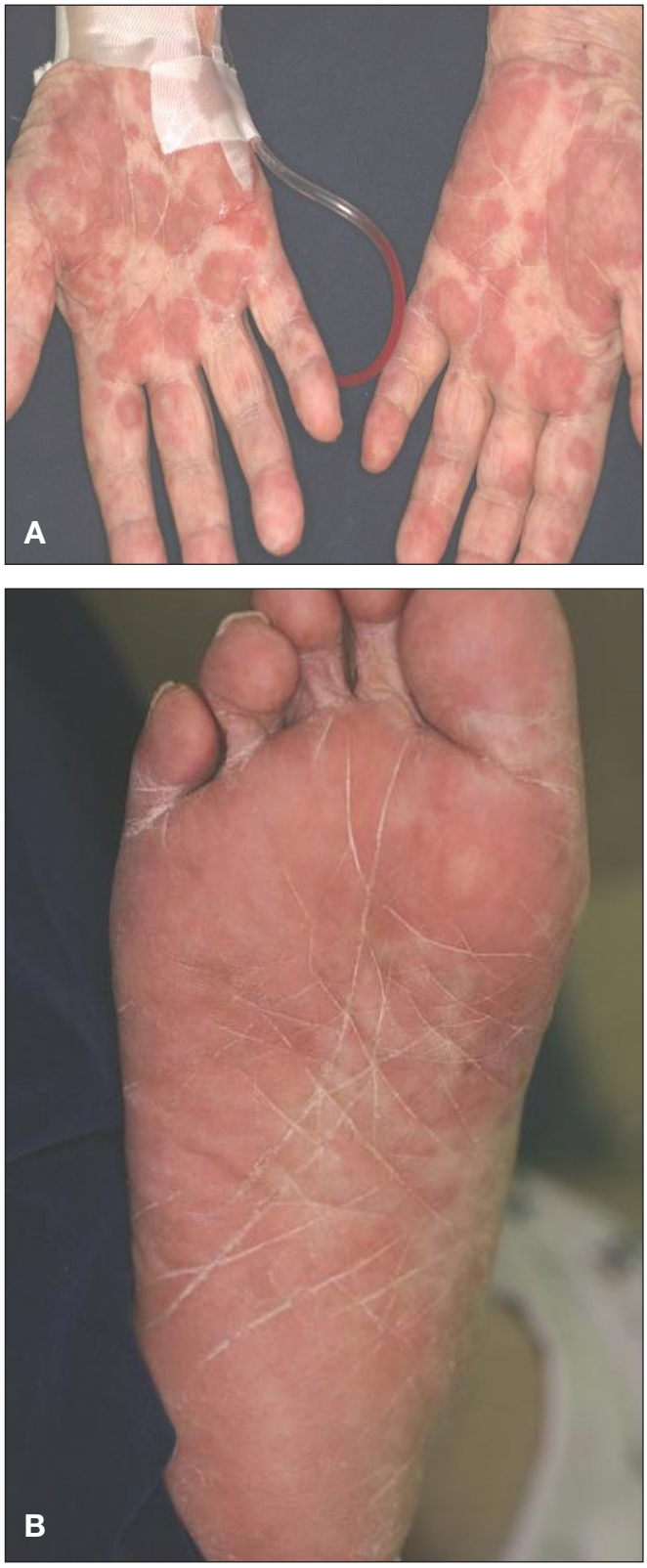

Fig. 1 - Erythematous macular rash on both palm (A) and sole (B) after 2 days of icodextrin dialysis.

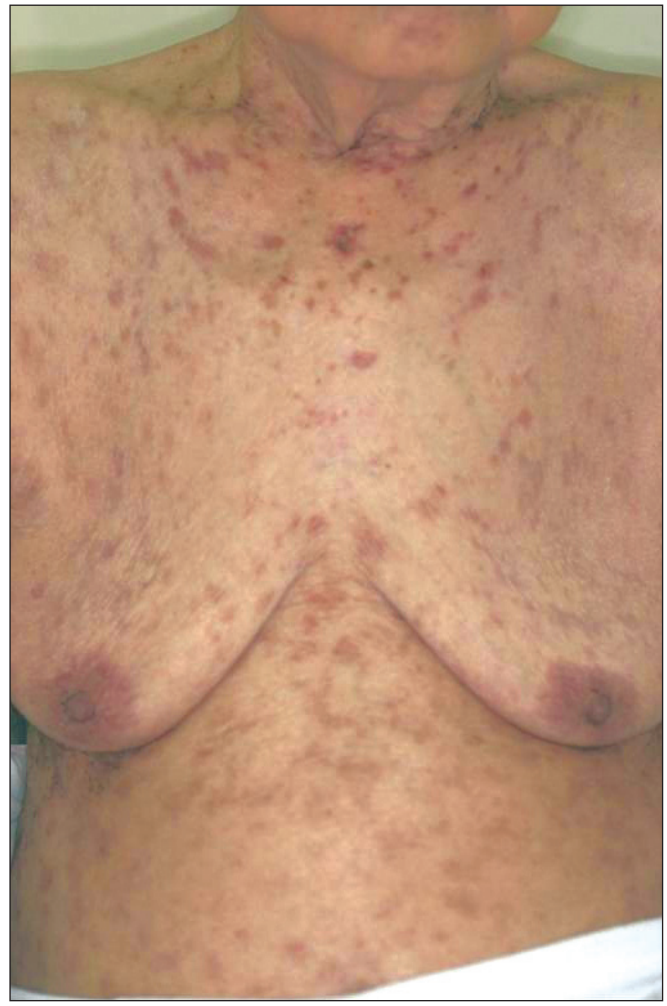

Fig. 2 - Erythematous crusted vesicles with pustules on trunk after 2 days of icodextrin dialysis.

with diuretics, an angiotensin II receptor blocker and a calcium channel blocker. However, symptomatic relief was not obtained by conventional therapies, and symptoms of congestive heart failure (CHF) increased until the patient suffered severe respiratory insufficiency even at rest. CAPD using standard glucose PD solution was initiated to remove excess fluid and manage refractory CHF after 1 month of conservative treatment. The patient's generalized edema and her clinical condition improved after initiation of CAPD. After discharge from hospital, she was maintained on CAPD using standard glucose PD solutions. A few months later, she became noncompliant with her low salt diet and frequently needed exchanges using hypertonic PD solutions despite the low average peritoneal transport characteristics. Thus, overnight exchange using icodextrin-based dialysate (Extraneal, lot number S05F20042) was prescribed to maintain euvolemia. The patient complained of pruritus immediately after infusion of icodextrin PD solution

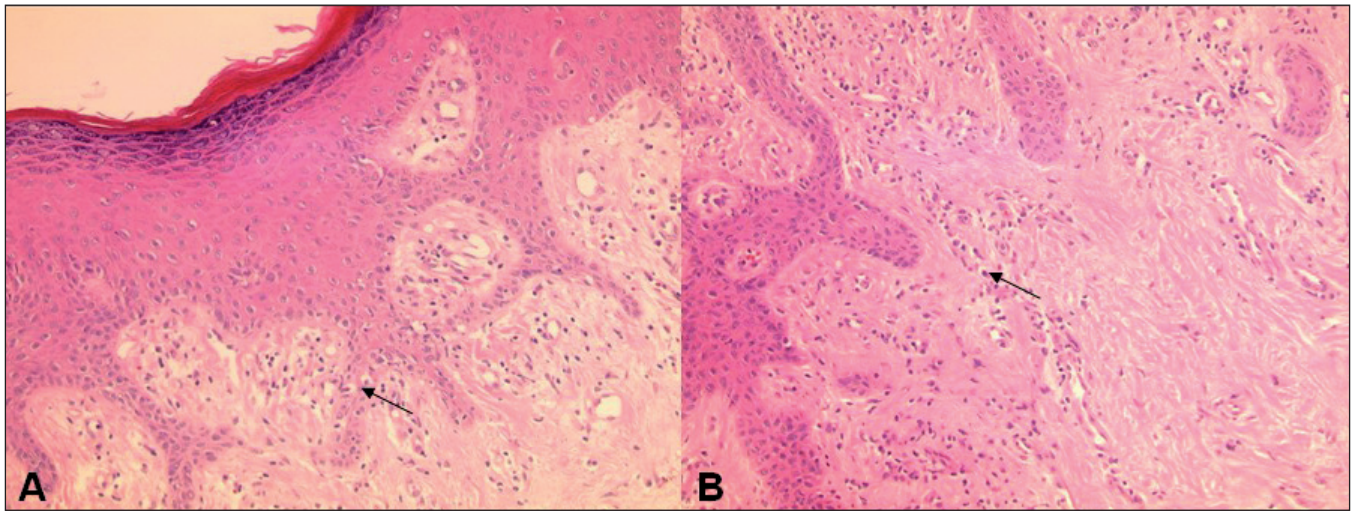

Fig. 3 - Palm skin shows interface dermatitis, basal vacuolization (A, arrow) and mild superficial perivenular lymphocytic infiltration (B, arrow) (H & E, ×200).

and started to develop a pruritic erythematous skin rash which later spread to the whole body after 2 days. The skin lesion initially started on her palms, soles, and face (Figs. 1A and B) and then spread to the trunk of the whole body (Fig. 2). Laboratory findings showed no signs of infection or inflammation, and PD effluents at the onset of the symptoms revealed no signs of peritoneal inflammation (WBC count <10 with no eosinophils). Skin biopsy on her palm showed basal vacuolization, interface dermatitis and mild superficial perivenular lymphocytic infiltration compatible with erythema multiforme (Fig. 3). Chronology of her symptoms strongly suggested adverse reaction to icodextrin, and icodextrin-based PD solution was discontinued. Conservative treatment using antihistamine, topical steroid agent and a low-dose oral steroid was prescribed, and the erythematous skin rash and pruritus gradually disappeared within 7 days after discontinuation of icodextrin. Currently she is clinically stable without edema using standard glucose PD solutions.

Discussion

The safety data from the clinical trials provide evidence that icodextrin PD solution is a well-tolerated dialysate with an adverse event profile generally similar to that of glucose-based solutions, with a few notable exceptions. Skin rash was a common treatment-related adverse reaction to icodextrin in various clinical trials (1, 2). Patients on icodextrin PD solution showed a higher incidence of rash (10.1%) compared with those on glucose-based PD solutions for the long-term (4.6%, $p<0.003$) (2). The rash related to icodextrin usually occurred in the first 3 weeks of treatment and involved the palms and soles and was mild or moderate in the majority of the patients. However, rare reports of severe exfoliative or psoriasiform dermatitis occurring early after initiation of icodextrin dialysis have been reported in the literature. In those reports the onset of the severe adverse skin reactions occurred usually between 4 and 12 days after initiation of icodextrin PD solution (3-9). In our case, the patient complained of generalized pruritus immediately after changing from the glucose-based solution to the icodextrin PD solution and developed generalized erythematous skin rash. Her medications had been unchanged for many weeks, and she had reported no previous history of allergic reactions to drugs.

The underlying mechanism of the severe cutaneous hypersensitivity to icodextrin is still unknown. Icodextrin is a glucose polymer that is metabolized to maltose and is structurally similar to the naturally occurring dextran, which can be responsible for a variety of allergic reactions including anaphylactoid or anaphylactic reactions (10, 11). The 2 polymers differ only in their linkage of glucose molecules: α1,4 for icodextrin and α1,6 for dextran. Patients who are chronically exposed to dextran treatment may show dextran deposition in the skin and peripheral nerves. This may cause stimulation of the cutaneous nerves and result in pruritus (12, 13). High titer of dextran reactive immunoglobulin G can be found in many of these patients (14), and the proportion of patients who have allergic reactions can be reduced substantially by use of hapten inhibition (15). However, no icodextrin reactive antibodies were demonstrated in previous cases, and clinical pictures of severe cutaneous reaction to icodextrin are not compatible with dextran-

induced anaphylactic reactions. Our case also failed to demonstrate any cause for adverse skin reactions to icodextrin. Probably unknown biochemical mechanisms or an immune response is associated with these variable clinical manifestations.

The present case is the first report of severe cutaneous reaction to icodextrin PD solution in Korea. The safety and efficacy of icodextrin PD solution has been documented through various clinical trials over the past decade. However, the possibility of adverse cutaneous reaction to icodextrin as in this patient should always be borne in mind.

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Received: February 06, 2006
Revised: June 12, 2006
Accepted: July 04, 2006