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Drug Rash With Eosinophilia and Systemic Symptoms Syndrome Induced by Chloral Hydrate in Early Childhood

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Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome, also known as drug-induced hypersensitivity syndrome (DIHS), is a rare, acute and severe life-threatening systemic disease. DRESS syndrome is characterized by fever, lymphadenopathy, rash, hypereosinophilia and involvement of systemic organs. The most commonly implicated drugs are anticonvulsants, sulfonamides and allopurinol. Chloral hydrate is a sedative and hypnotic drug frequently used in pediatric patients. We first report a case of DRESS syndrome induced by chloral hydrate in a 14-month-old female.

Key Words: Drug hypersensitivity; chloral hydrate

INTRODUCTION

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome, also known as drug induced hypersensitivity syndrome (DIHS), is a type of adverse drug reaction, which is a severe life threatening systemic disease that should be differentiated from Stevens-Johnson syndrome and toxic epidermal necrolysis.[1,2] The primary clinical manifestations are fever, lymphadenopathy, rash, hypereosinophilia, and involvement of systemic organs. Systemic organ involvement can present as hepatitis, interstitial pneumonia, interstitial nephritis, and carditis.[2,3] The mortality of DRESS syndrome is approximately 10%.[3] The most commonly implicated drugs are anticonvulsants, sulfonamides and allopurinol.[4,5] Dress syndrome may occur in children, but most cases occur in adults.[5] Chloral hydrate is a sedative and hypnotic drug, frequently used for purpose of examination in pediatric patients. It is known as safe drug and hypersensitivity reaction is very rare.[6,7] To the best of our knowledge, DRESS syndrome related to chloral hydrate has not been reported previously. We report the first case of DRESS syndrome induced by chloral hydrate in early childhood.

CASE REPORT

A 14-month-old female was referred to Department of Pediatrics after a total correction of tetralogy of Fallot. Her conditions were fair with stable vital signs after the operation. Until recently, the following drugs were used for the operation and cardiac catheterization: ceftizoxime, cefixime, cefazedone, furosemide, spironolactone, tranexamic acid, protamine sulfate, mannitol, ranitidine, and methylprednisolone. Chloral hydrate was administered 3 weeks prior to her visit for preoperative echocardiography. There was no history of adverse reactions or hypersensitivity. On postoperative day 7, she had a good condition and there were not abnormal laboratory findings. She was administered 500 mg of chloral hydrate (Pocral®, 50 mg/kg/dose) for echocardiography. The rash appeared abruptly 10 hours later. Her body temperature was 38.3°C, blood pressure 90/60 mmHg, heart rate 184 beats per minute and oxygen saturation 94%. Erythematous maculopapular eruption had spread from the face and trunk to the extremities within 4 days. On the fifth day after administration of chloral hydrate, the fever persisted and oliguria (<1 mL/kg/hr) and generalized edema progressed. She was diagnosed with hepatosplenomegaly (Fig. 1). Interstitial pneumonia was observed on the chest radiography (Fig. 2). Laboratory findings showed hepatitis (AST 182 IU/L [10-40 IU/L], ALT 109 IU/L [10-40 IU/L]), hyperbilirubinemia (total bilirubin 2.9 mg/dL [0.3-1.3 mg/dL], direct bilirubin 1.04 mg/dL [0.05-0.40 mg/dL]), leukocytosis (white blood cell 38,300 /μL [6,000-15,000 /μL]), atypical lymphocytosis (4,213 /μL, 11%), hypereosinophilia (eosinophil 1,630 /μL, 5%), and proteinuria. Immunoglobulin G (258 mg/dL [700-1,600 mg/dL]), Immunoglobulin M (30 mg/dL [40-230 mg/dL]), and Immunoglobulin A (6.2 mg/dL [70-400

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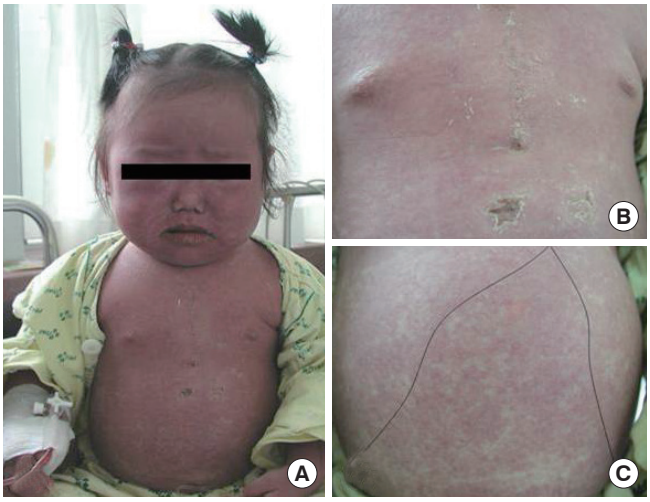

Fig. 1. (A) Clinical photographs show generalized edematous features & systemic morbilliform rash as DRESS syndrome. (B) Sternostomy wounds were observed and (C) hepatosplenomegaly was detected.

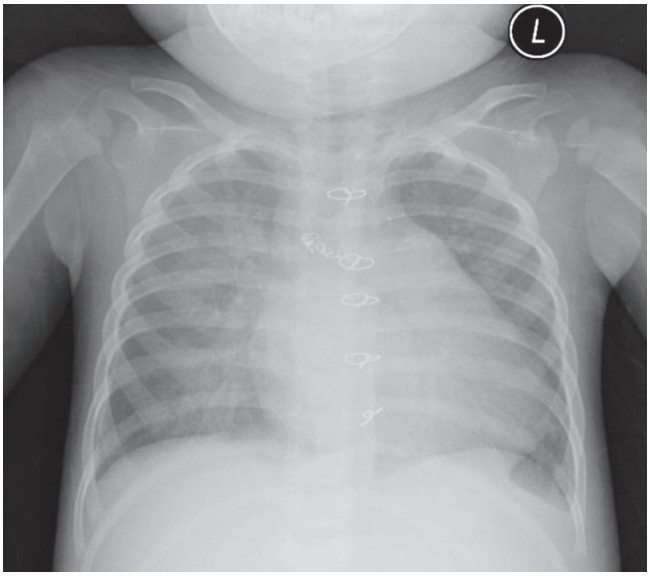

Fig. 2. Chest radiograph shows increased ground glass opacity in the whole lung field, which represents interstitial pneumonia.

mg/dL]) were decreased. Antinuclear antibody was negative. Pathogens were not isolated from blood, urine, or stool culture. Serologic tests for Epstein–Barr virus, cytomegalovirus, Measles virus, Hantaan virus, Leptospira, and Scrub typhus were negative. At this time, DRESS syndrome was diagnosed. However, the responsible drug remained unclear. Oral prednisolone (1 mg/kg/day) was administered daily for 14 days and was then tapered for 7 days. During a 2-month follow-up period, clinical symptoms, laboratory tests and chest radiography returned to normal.

After the fourth month, she visited the outpatient clinic for a follow-up echocardiography, and was again administered chloral hydrate. Three days later, fever, generalized whole body rash with edema of the face, hypereosinophilia, oliguria, hepatitis, and interstitial pneumonia occurred again. Recurrent DRESS syndrome induced by chloral hydrate was diagnosed and oral prednisolone was administered. The patient recovered within 7 days. During the next 3 years, the patient was followed and did not show any complications.

DISCUSSION

DRESS syndrome is a rare, potentially life-threatening, drug-induced hypersensitivity reaction that includes rash, hematologic abnormalities, lymphadenopathy, and internal organ involvement.[3,5] Several drugs cause DRESS syndrome, including carbamazepine, sulfasalazine, allopurinol, phenobarbital, hydroxychloroquine, and lamotrigine.[5] To our knowledge, this is the first case of DRESS syndrome induced by chloral hydrate in early childhood. Our patient was classified as a definitive DRESS case according to the RegiSCAR scoring system.[5] Furthermore, re-exposure to chloral hydrate confirmed the diagnosis.

Typically, DRESS syndrome has a latency period (usually 2-6 weeks) after use of a culprit drug.[8] A retrospective study showed that the average interval time to drug reaction was 20.7 days (range, 3-76 days).[9] In our case, Chloral hydrate administered twice (3 weeks and 10 hours ago) before the first episode. Drug which is administered 3 weeks ago may induce DRESS syndrome but it is not clear. In the second episode, latency period between drug exposure and onset of symptoms was 3 days, which is relatively short.

The pathophysiology of DRESS syndrome is unclear. It is suggested that there is primarily drug-specific immune reaction acting as trigger of viral reactivation (*e.g.* human herpes virus 6, human herpes virus 7, Epstein- Barr virus) by as yet unknown mechanisms.[8-13] Previous reports indicated that causative drugs have in common intrinsic properties to potentially cause transient immune dysfunction.[10-13] It has also been demonstrated that there is a decrease in serum immunoglobulin levels at onset in patients with DRESS.[11] In our case, human herpes virus was not checked, however, immunoglobulin levels were decreased in the first episode. During a follow-up period, Immunoglobulin returned to normal.

The use of systemic corticosteroids for the treatment of DRESS syndrome with severe organ involvement has not been evaluated in randomized trials. However, there is general consensus among experts on the use of systemic corticosteroids for the treatment of DRESS syndrome with severe organ involvement, particularly in patients with renal and/or pulmonary involvement.[5,9,13] In the second episode of this case, early treatment with systemic corticosteroids decreased symptom duration. Thus, early treatment with steroids could be used to treat DRESS syndrome.

We report the first case of DRESS syndrome induced by chlo-

ral hydrate in early childhood. In pediatric patients, chloral hydrate is a commonly used sedative. Thus, clinicians should consider DRESS syndrome for patients who have taken chloral hydrate.

REFERENCES

1. Bonnetblanc JM. Drug hypersensitivity syndrome. Dermatology 1993;187:84-5.
2. Roujeau JC, Stern RS. Severe adverse cutaneous reactions to drugs. N Engl J Med 1994;331:1272-85.
3. Bocquet H, Bagot M, Roujeau JC. Drug-induced pseudolymphoma and drug hypersensitivity syndrome (drug rash with eosinophilia and systemic symptoms: DRESS). Semin Cutan Med Surg 1996;15:250-7.
4. Pellock JM. Carbamazepine side effects in children and adults. Epilepsia 1987;28 Suppl 3:S64-S70.
5. Cacoub P, Musette P, Descamps V, Meyer O, Speirs C, Finzi L, Roujeau JC. The DRESS syndrome: A literature review. Am J Med 2011;124:588-97.
6. Lipshitz M, Marino BL, Sanders ST. Chloral hydrate side effects in young children: causes and management. Heart Lung 1993;22:408-14.
7. Heistein LC, Ramaciotti C, Scott WA, Coursey M, Sheeran PW, Lemler MS. Chloral hydrate sedation for pediatric echocardiography: physiologic responses, adverse events, and risk factors. Pediatrics 2006;117:e434-41.
8. Descamps V, Valance A, Edlinger C, Fillet AM, Grossin M, Lebrun-Vignes B, Belaich S, Crickx B. Association of human herpesvirus 6 infection with drug reaction with eosinophilia and systemic symptoms. Arch Dermatol 2001;137:301-4.
9. Chen YC, Chiu HC, Chu CY. Drug reaction with eosinophilia and systemic symptoms: a retrospective study of 60 cases. Arch Dermatol 2010;146:1373-9.
10. Kano Y, Hiraharas K, Sakuma K, Shiohara T. Several herpesviruses can reactivate in a severe drug-induced multiorgan reaction in the same sequential order as in graft-versus-host disease. Br J Dermatol 2006;155:301-6.
11. Tohyama M, Hashimoto K, Yasukawa M, Kimura H, Horikawa T, Nakajima K, Urano Y, Matsumoto K, Iijima M, Shear NH. Association of human herpesvirus 6 reactivation with the flaring and severity of drug-induced hypersensitivity syndrome. Br J Dermatol 2007;157:934.
12. Kano Y, Inaoka M, Shiohara T. Association between anticonvulsant hypersensitivity syndrome and human herpesvirus 6 reactivation and hypogammaglobulinemia. Arch Dermatol 2004;140:183-8.
13. Walsh SA, Creamer D. Drug reaction with eosinophilia and systemic symptoms (DRESS): a clinical update and review of current thinking. Clin Exp Dermatol 2011;36:6-11.