Sodium nitroprusside and toxic epidermal necrolysis

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Summary

Sodium nitroprusside (SNP) is one of the most widely used parenteral antihypertensive agents in severe hypertension management. Toxic epidermal necrolysis (TEN) is a rare, mostly drug-induced, severe muco-cutoneous reaction with various complications and high mortality.

A fifteen years old girl who is on hemodialysis for chronic renal insufficiency and was hospitalized for emergency management of hypertension, developed a diffuse maculopapular rash within minutes after SNP infusion. In 72 hours, approximately 40% of the body surface was involved with skin detachment indicating epidermal necrolysis and a skin biopsy confirmed the diagnosis of TEN.

To the best of our knowledge there is no report of an association of SNP and TEN in the English literature and the clinical data exemplifying consequent IgE and non-IgE mediated hypersensitivity reactions are scanty. With this report we wanted to present a rare complication of SNP infusion indicating another rare occurrence of sequential IgE and non-IgE mediated hypersensitivity reactions. ***(Asian Pac J Allergy Immunol 2012;30:243-5)***

Key words: *sodium nitroprusside, toxic epidermal necrolysis, hypertension, drug allergy, child*

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Introduction

Sodium nitroprusside (SNP) is an intravenously administered antihypertensive agent producing powerful venous and arterial dilatation. It acts directly on the smooth muscle of blood vessels affecting both resistance and capacitance vessels in a dose dependent manner. The most frequent side effects of SNP are associated with its end-products which are cyanide radicals. Central nervous system dysfunction, cardiovascular instability and metabolic acidosis may be seen in this spectrum.[1]

Toxic epidermal necrolysis (TEN) is a rare, mostly drug-induced, severe muco-cutaneous reaction with various complications and a high mortality rate. Until now more than 200 therapeutic agents have been reported as causative factors in the etiology of TEN.[2]

In this report we present a patient with chronic renal failure who developed TEN after SNP infusion. We want to report this case for two reasons: firstly this is the first case of TEN due to SNP and secondly, this case is a clinical example of concurrent IgE mediated and non-IgE mediated reactions.

Case report

A 15 year old girl with chronic renal failure was admitted to hospital complaining of a headache of three days duration. She had been on the hemodialysis programme and had been taking three anti-hypertensive drugs (amlodipine, enalapril and doxazosin) along with other chronic kidney disease supportive treatment. She had had no additional medication for three months.

On admission her blood pressure was 200/150 mmHg and we decided to use intravenous SNP to treat her symptomatic and severe hypertension in a dose of 0.3 µg/kg/min. At the third minute of the infusion a maculopapular pruritic rash appeared and the infusion was stopped. About 36 hours after taking the SNP she developed oral lesions, generalized erythema and bullous lesions on her hands and wrists. In the next 24 hours the bullous lesions became generalized and then skin detachments occurred at the sites where these lesions first appeared (Figure1). Within three days

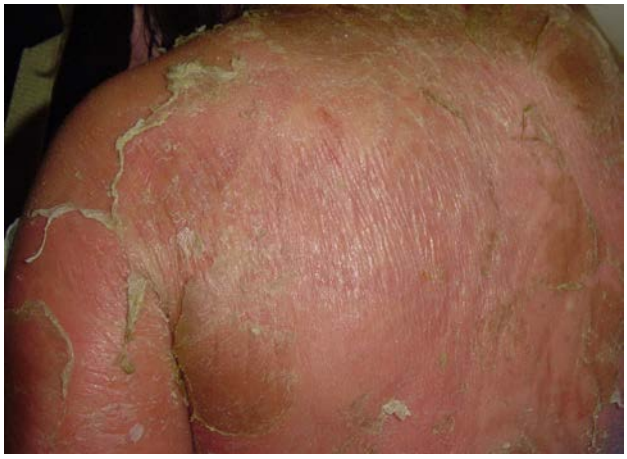

Figure 1. Skin detachment on the shoulders and back

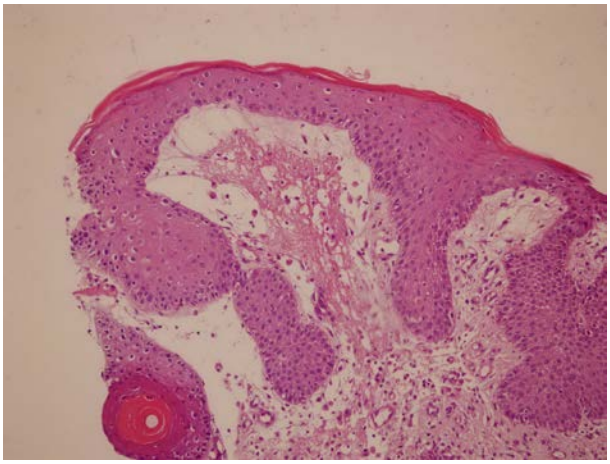

Figure 2. Subepidermal blister formation with necrotic keratinocytes on the roof of the bullae

the extent of the bullous lesions was greater than 40 percent of her body surface. After the reaction she said that she had had a cutaneous reaction after taking SNP last year.

Laboratory investigations showed leukocytosis with eosinophilia (900/mm^3), elevated acute phase reactants including erythrocyte sedimentation rate and C-reactive protein. Blood and urine cultures were negative. The skin biopsy from the left upper leg demonstrated sub-epidermal cleavage and necrosis of keratinocytes on the roof of bullae (Figure 2). These clinical findings and the pathological picture were consistent with a diagnosis of TEN.

Following initial fluid and electrolyte management, intravenous immunoglobulin treatment was given for three days in a dose of 0.5 g/kg/day. Because of the high secondary bacterial infection risk in these patients, dressings were done with sterile covers and wide spectrum antibiotics were also included in the management.

Her symptoms associated with TEN resolved in two weeks. Her eye examination was normal. On the 27th hospital day she was discharged without any complications.

Discussion

Toxic epidermal necrolysis is a severe, potentially life threatening systemic disease which was firstly described in 1956 by Lyell.[3] It is most commonly drug-related but infectious agents may be responsible as a causative factor.[4] The incidence of TEN is estimated at 0.4 to 1.3 cases per million persons per year.[5]

Toxic epidermal necrolysis is considered to be a T cell mediated disorder which consists of activation of CD8 T lymphocytes leading to destruction and apoptosis of keratinocytes.[5,6] The pathogenesis of TEN includes increased expression of keratinocyte membrane bound Fas and Fas-ligand and keratinocyte apoptosis occurs through this processes.[7]

Our patient noticed that she had a cutaneous reaction after taking SNP the previous year but she only revealed this after the reaction. Therefore we thought that the initial cutaneous signs which appeared within three minutes were associated with an IgE mediated hypersensitivity reaction. The level of serum total IgE was normal but we know that the important serologic marker for diagnosis of type 1 hypersensitivity reactions is drug specific IgE. Unfortunately there is no appropriate test for evaluation of this marker for SNP. We also could not perform a drug provocation test with SNP since the patient had had a severe, life threatening reaction (TEN).[8] In addition to the first reaction, the time course of the second reaction strongly suggested SNP as the responsible agent.

There are few data about concurrence of IgE mediated and non-IgE mediated reactions in the literature.[9] Furthermore, a lot of drugs are incriminated as a trigger of TEN but to our knowledge there is no report about SNP associated TEN in the literature. For these reasons we want to draw attention to the fact that SNP may cause TEN and that two different types of hypersensitivity reaction may be seen together.

References

1. Friederich JA, Butterworth JF 4th. Sodium nitroprusside: twenty years and counting. Anesth Analg. 1995;81:152-62.
2. Koh MJ, Tay YK. Stevens-Johnson syndrome and toxic epidermal necrolysis in Asian children. J Am Acad Dermatol. 2010;62:54-60.
3. LYELL A. Toxic epidermal necrolysis: an eruption resembling scalding of the skin. Br J Dermatol. 1956;68:355-61.
4. Forman R, Koren G, Shear NH. Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis in children: a review of 10 years' experience. Drug Saf. 2002;25:965-72.
5. Letko E, Papaliodis DN, Papaliodis GN, Daoud YJ, Ahmed AR, Foster CS. Stevens-Johnson syndrome and toxic epidermal necrolysis: a review of the literature. Ann Allergy Asthma Immunol. 2005;94:419-36.
6. Kehren J, Desvignes C, Krasteva M, Ducluzeau MT, Assossou O, Horand F, et al. Cytotoxicity is mandatory for CD8(+) T cell-mediated contact hypersensitivity. J Exp Med. 1999;189:779-86.
7. Paul C, Wolkenstein P, Adle H, Wechsler J, Garchon HJ, Revuz J, et al. Apoptosis as a mechanism of keratinocyte death in toxic epidermal necrolysis. Br J Dermatol. 1996;134:710-4.
8. Gruchalla RS, Pirmohamed M. Clinical practice. Antibiotic allergy. N Engl J Med. 2006;354:601-9.
9. Lam A, Randhawa I, Klaustermeyer W. Cephalosporin induced toxic epidermal necrolysis and subsequent penicillin drug exanthem. Allergol Int. 2008;57:281-4.