Drug-induced hypersensitivity syndrome accompanied with acute renal failure with hemodialysis: A case and literature review

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Abstract

Drug-induced hypersensitivity syndrome (DIHS) is a severe type cutaneous adverse event involving systemic organ failures. In some cases of DIHS, an acute renal failure takes place and it becomes a necessary to perform hemodialysis. However, the clinical outcome of renal failure in the course of treatment of DIHS remains unclear. Herein, we report a case of DIHS complicated with acute renal failure, which requires hemodialysis: A 72-years-old male had initiated to take allopurinol for his gout, and recognized erythematous eruption on his trunk and extremities 28 days after allopurinol administration. He also recognized edema in extremities 36 days after the treatment. From the clinical course and laboratory examination, we speculated his skin eruption as drug-induced hypersensitivity syndrome possibly due to allopurinol. Therefore, 40mg oral prednisolone was administrated for his skin eruption. Furthermore, hemodialysis was administrated twice a week. Hemodialysis was ceased 11 days after hemodialysis administration. Allopurinol showed a positive reaction in lymphocyte stimulation test, which was performed by were performed at SRL, Inc., (Tokyo, Japan). Based on these laboratory examinations, we finally diagnosed his skin eruption as drug-induced hypersensitivity syndrome due to allopurinol. Furthermore, we also review the DIHS cases accompanied with acute renal failure with hemodialysis in English literatures.

Introduction

Drug-induced hypersensitivity syndrome (DIHS) is a severe type cutaneous adverse event involving systemic organ failures [1]. In some cases of DIHS, an acute renal failure takes place and it becomes a necessary to perform hemodialysis [2] [3]. However, the clinical outcome of renal failure in the course of treatment of DIHS remains unclear. Herein, we report a case of DIHS complicated with acute renal failure, which requires hemodialysis. Furthermore, we also review the DIHS cases accompanied with acute renal failure with hemodialysis in English literatures.

Case Presentation
A 72-years-old male had initiated to take allopurinol for his gout, and recognized erythematous eruption on his trunk and extremities 28 days after allopurinol administration. He also recognized edema in extremities 36 days after the treatment. He was also administrated anti-hypertensive agents several years ago. He was referred to our department for evaluation of his skin eruption. Physical examination showed infiltrated erythematous plaques and papules located on his trunk and extremities (Figure 1A). He had a high fever (38.1 °C). There was no involvement of mucosal lesion. A skin biopsy taken from his erythematous eruption revealed that a lymphocyte infiltration in the dermis without dyskeratotic keratinocyte in the epidermis (Figure 1B). Laboratory examination revealed that elevated aspartate aminotransferase 616 U/l, and alanine aminotransferase 776 U/l. White blood cell count increased at 19600/μl with elevation of eosinophils (11.0
% and atypical lymphocytes (9.0 %). His renal dysfunction gradually developed showing an elevation of serum creatine (2.64 mg/dl). From the clinical course and laboratory examination, we speculated his skin eruption as drug-induced hypersensitivity syndrome possibly due to allopurinol. Therefore, 40mg oral prednisolone was administrated for his skin eruption. Furthermore, hemodialysis was administrated twice a week. Hemodialysis was ceased 11 days after hemodialysis administration. However, his skin eruption and renal dysfunction were improved by the treatment. After 4 weeks the HHV-6-IgG titer was increased from 1:10 to 1:80. Allopurinol showed a positive reaction in lymphocyte stimulation test, which was performed by were performed at SRL, Inc., (Tokyo, Japan). Therefore, lymphocyte stimulation test using the metabolite of allopurinol, oxypurinol, was not performed. Based on these laboratory examinations, we finally diagnosed his skin eruption as drug-induced hypersensitivity syndrome due to allopurinol.

**Discussion**

Although DIHS is sometimes complicated with acute renal failure, hemodialysis administration for acute renal failure following DIHS are a rare event. Because the detail clinical characteristics of these cases, especially the prognosis, remained unclear, we review the cases in English and Japanese case report literatures [2] [3] [4] [5] (Table 1). There have been 6 reported cases including our case. The male: female ratio is 2: 1, and the mean age is 57.8 years. The causative agents are not specific agents and wide variety of drugs become the causative agent to cause acute renal failure with hemodialysis administration following DIHS. Average interval of the initiation of drug intake and appearance of drug eruption and acute renal failure are 23.0 days and 46.3 days, respectively. Therefore, renal dysfunction was recognized 3 weeks after the appearance of following skin eruptions in average. All cases well responded to hemodialysis and they stop using hemodialysis shortly, suggesting a possible favorable clinical behavior in these cases.

Although the pathogenesis of acute renal failure following DIHS remains unclear, almost all cases of causative agent’s metabolism pathway is urinary excretion, excluding metronidazole. Therefore, it is assumed that causative agent might also exacerbate immunological reaction in kidney. Interestingly, it has also been reported that lymphocyte stimulation test is also helpful for finding the causative agent in drug-induced acute renal failure [6]. Furthermore, allopurinol excretes uric acid to renal tubules. These uric acids exacerbate innate immune response-related inflammation through NALP3 inflammasome activation in renal tubules.

![Table 1](https://example.com/table1.png)

**TABLE 1: Review of the cases of hemodialysis administration for acute renal failure following DIHS**

**Conclusions**

Taken together, the combinations of allergic and innate immune inflammations might contribute to the pathogenesis of acute renal failure following allopurinol-induced DIHS. No specific causative agent has been identified in our literature review, clinician should be kept in mind the risk of severe acute renal failure who might need hemodialysis during the clinical course. Since the limited number of cases need the haemodialysis in acute renal failure in DIHS cases, further detail mechanism or characteristics of acute renal failure in patients with DIHS is necessary to be clarified by further investigation.

**Additional Information**

**Disclosures**

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**Author** | **Sex** | **Age** | **Causative agent** | **Interval period from causative agent administration** | **Outcome of renal failure**
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Higuchi M, et al. [2] | Male | 53 | Diaphenylsulfone | Drug eruption: 28 days; Acute renal failure: 47 days | Hemodialysis off
Augusto JF, et al. [4] | Female | 77 | Sulphasalazine | Drug eruption: 28 days; Acute renal failure: 50 days | Hemodialysis off
Chia-Chun Ang, et al. [5] | Male | 32 | Ciprofloxacin, or metronidazole | Drug eruption: 3 days; Acute renal failure: N.D | Hemodialysis off
| Female | 84 | Metformin | Drug eruption: 7 days; Acute renal failure: N.D | Hemodialysis off
Our case | Male | 72 | Allopurinol | Drug eruption: 28 days; Acute renal failure: 36 days | Hemodialysis off
N.D, not described
**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

**References**


