

Steven-Johnson syndrome and toxic epidermal necrolysis in Northern Sarawak between year 2011 and 2015: A retrospective review of causative agents and clinical outcome

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Abstract *Objective* To determine the causes and treatment outcome of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).

Methods A retrospective review was conducted on SJS and TEN cases admitted to Miri General Hospital between year 2011 and 2015.

Results Total of ten patients were admitted in five years period, nine cases of SJS and one case of TEN with highest number recorded in 2014 (4 cases). The commonest causative agent was allopurinol (30%). Among the ten cases, 7 patients were given steroids, 1 patient given intravenous immunoglobulin (IVIG), 2 patients given both steroids and IVIG. There was a case mortality from SJS secondary to allopurinol after 38 days of admission and patient was given only corticosteroids.

Conclusion Allopurinol is the most common causative agent with mortality in Miri General Hospital. Allopurinol should be used judiciously. Combination therapy had tendency to reduce mortality rate in comparison with corticosteroid therapy alone. However, in view of small sample size, efficacy and superiority between treatment of corticosteroids and IVIG cannot be assessed.

Key words

Steven-Johnson syndrome, toxic epidermal necrolysis, drug reaction, steroids, intravenous immunoglobulin.

Introduction

Stevens-Johnson syndrome (SJS) and Toxic epidermal necrolysis (TEN) are severe adverse cutaneous drug reaction characterized by epidermal loss and multisite mucositis.^{1,2} SJS and TEN are spectrum of disease with different severity. According to study by Bastuji-Garin *et al.*³ patients with SJS have epidermal

detachment <10% of body surface area (BSA) plus widespread purpuric macules or flat atypical targets; overlap SJS-TEN with detachment of 10-30% BSA plus widespread purpuric macules or flat atypical targets and TEN with spots, detachment >30% BSA plus widespread purpuric macules or flat atypical targets and TEN without spots, detachment > 30% BSA with loss of large epidermal sheets without purpuric macules or target lesions. Etiology of this disorder is usually drug-related, however, other causes e.g. infectious diseases are found to be related where *Mycoplasma pneumonia* being the most commonly

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reported.^{4,5,6}

The aim of this study was to determine the causes and treatment outcome of SJS and TEN cases admitted to Miri General Hospital between year 2011 and 2015.

Methods

A retrospective review of all patients with the diagnosis of SJS and TEN who had been admitted to Miri General Hospital between year 2011 and 2015 was done. All cases were identified from the medical wards' census. Medical records were retrieved to obtain the following data: patient demographics, comorbid, causative agents, extent of mucocutaneous involvement, duration of hospital stay, treatment given and treatment outcome. Relevant data were tabulated and analyzed using SPSS version 16.0.

Results

Patients clinical data During the five-year period, nine cases of SJS and one case of TEN were admitted, the highest number recorded in 2014 (4 cases). Six of them were females. 30% of patients had underlying diabetes mellitus (Table 1).

Causes of SJS and TEN All of the ten cases were found to be drug-related. Major culprits are allopurinol (30%) and anticonvulsants (30%), (Table 2).

Treatment regimes and outcomes Among the ten cases, seven patients were given steroids, one patient given intravenous immunoglobulin (IVIG), two patients given both steroids and IVIG. Duration of hospital stay ranged from 4 to 38 days. There was a case mortality from SJS

Diabetes mellitus	3 (30)
Hypertension	1 (10)
Dyslipidemia	1 (10)
Pulmonary tuberculosis	1 (10)
Retroviral disease	1 (10)
Epilepsy	1 (10)
None	2 (20)

Table 2: Causative agents of SJS and TEN (n=10).

Causative Agent	N (%)
Allopurinol	3 (30)
Carbamazepine	2 (20)
Phenytoin	1 (10)
Antimicrobial	1 (10)
Antiretroviral (Nevirapine)	1 (10)
Traditional medicine	2 (20)

secondary to allopurinol after 38 days admission due to sepsis. The patient was given only corticosteroid.

Discussion

SJS and TEN are rare but life-threatening conditions and have significant healthcare burden. A recent study in United States showed that mean adjusted mortality was 4.8% for SJS, 19.4% for SJS/TEN, and 14.8% for TEN.⁷

Allopurinol was the most common causative agent of SJS and TEN in Miri General Hospital. This was similar to EuroSCAR study where allopurinol was the most common causative agents due to increasing usage and dosage of this drugs.⁸ HLA B5801 allele was found to be strongly associated with adverse cutaneous drug reaction caused by allopurinol among Han Chinese and Japanese patients.^{9,10} Anticonvulsants were found to be second most common causative agents in this study.

Management of SJS and TEN involves removal of causative agents, supportive care and specific treatment. The definitive treatment for SJS/TEN is still controversial.^{11,12} Treatment modalities include corticosteroids, plasmapheresis and IVIG. Few recent studies suggested that corticosteroids usage is valid treatment for SJS

Table 1 Patients' comorbid (n=10).

Comorbid	N (%)
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and TEN.¹³⁻¹⁵ Besides, early application of steroids provided beneficial effects, and that combination therapy with steroids and IVIG showed better therapeutic effects than did steroids alone.¹⁶ 90% of patients in present study were on corticosteroids and two patient were given combination therapy.

However, the efficacy and superiority between treatment of corticosteroids and IVIG cannot be assessed in this study due to small sample size. Besides that, only hospitalized patients were included in this study, this may not provide the full evaluation as the majority of the patients with mild forms of disease are treated in primary care setting.

Conclusion

Allopurinol was the commonest causative agent of SJS and TEN in Miri General Hospital. Its usage should be used judiciously. Further well-designed studies are required to compare the efficacy of treatment between corticosteroids and IVIG.

How does this paper make a difference to general practice?

- Allopurinol was found to be leading cause of severe cutaneous adverse reaction.
- Usage of allopurinol should be with clear indication due to high risk of severe cutaneous adverse reaction.
- Start treatment with allopurinol at low dose, adjust dose and monitor closely.
- Education to patients and family members regarding early recognition of allergic reaction and discontinuation of drugs at first appearance of skin rash.

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