

Severe cutaneous adverse reactions: a 4-year experience in a tertiary referral hospital in Malaysia

Abstract

Introduction: Severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are related to a variety of drugs and are associated with significant morbidity and mortality. Awareness of local clinicoepidemiology of SCARs may play a vital role in future clinical management protocols.

Methodology: A retrospective review of all patients referred to the Department of Dermatology of Hospital Tengku Ampuan Afzan, Kuantan, and Pahang, Malaysia with confirmed SCAR from 2013 to 2016 was carried out to determine the epidemiologic pattern of SCARs in the local population.

Results: A total of 25 patients with 25 reactions were seen among 7,353 new patients, yielding an incident rate of 0.34% (yearly SCAR rate range: 0.38-0.56%), with the highest rate seen among indigenous peoples and Indians (0.63% and 0.62% respectively). SCARs (SJS, TEN, drug-related eosinophilia with systemic symptoms-DRESS, and acute generalized exanthematous pustulosis-AGEP) accounted for 40.3% of all cutaneous adverse drug reactions. SJS (15 cases) was the most frequent SCAR, followed by TEN (6), DRESS (2) and AGEP (2). 58.3% of patients were aged between 21 and 60 years, while the mean age was 53.7 years (range: 4-92). More females (80.0%) had SJS than males (20.0%), while TEN showed a reverse pattern (83.3% males vs. 16.7% females). Overall, the male: female ratio was 1:1.27. Allopurinol was the commonest culprit drug causing SJS (7/15) and TEN (2/6). Antimicrobials were the predominant group which contributed to 44.0% of SCARs. One-third of our patients only took a single drug, while another third took only two drugs. Two patients died, one each from DRESS and TEN, resulting in a mortality rate of 8.0%.^{1,2}

Conclusion: SJS was the commonest SCAR encountered in our center, while the commonest culprit drug was allopurinol. Antimicrobials as a group caused the most SCARs.

Keywords: drugs, allopurinol, symptoms, toxic epidermal, health care, patients

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Abbreviations: SCAR, severe cutaneous adverse reaction; SJS, stevens-johnson syndrome; TEN, toxic epidermal necrolysis; DRESS, drug-related eosinophilia with systemic symptoms; AGEP, acute generalized exanthematous pustulosis

Introduction

Severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug-related eosinophilia with systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP)³ are associated with significant morbidity and mortality. Awareness of local epidemiology of SCARs may play a vital role in prescribing practices by health care providers. Thus, a retrospective review of all patients referred to the Department of Dermatology of Hospital Tengku Ampuan Afzan, Pahang, Malaysia with confirmed SCAR from 2013 to 2016 was carried out to determine the epidemiologic pattern of SCARs in the local population. Out of 62 cases of cutaneous adverse drug reactions referred to the Department of Dermatology of Hospital Tengku Ampuan Afzan, Pahang, Malaysia over that period of time, 25 (40.3%) were SCAR, involving hospitalized patients. The high percentage is likely due to the hospital being the referral center for severe dermatology cases in the state. They were among 7,353 new patients seen during that period, yielding an incidence rate of 0.34% (yearly SCAR rate range: 0.38-0.56%).⁴ There were 15 cases (60%) of SJS, six (24%) TEN, and two (8%) each of AGEP and DRESS.

TEN was seen with equal frequency among Malays, Chinese and Indians, while the highest SCAR rate was seen among indigenous peoples (0.63%; $p=0.004$) (Table 1). 60.0% of patients with SCAR were between 21 and 60 years old, with a mean age of 53.7 years (range: 4-92).⁵

Two patients died, one each from DRESS and TEN, giving a mortality rate of 8.0%. More females (80.0%) had SJS than males (20.0%), while TEN showed a reverse pattern (83.3% males vs. 16.7% females); overall, the male: female ratio was 1:1.27. Allopurinol was the commonest culprit drug causing SJS (7/15) and TEN (2/6) while antimicrobials was the predominant group which contributed to 44.0% of SCARs, with Amoxicillin, Cotrimoxazole (3 cases each)⁶ and Dapsone (2 cases) being the most frequent causative agents. One-third of our patients only took a single drug, while another third took only two drugs. Where do we stand against other regional centers? Table 2 compares clinicoepidemiological studies on SCAR in Malaysia and various Asian countries. SJS was the commonest SCAR reported in centers in South-East Asia, India and China, and accounted for two-thirds of all SCARs observed in the three Malaysian hospitals above. The mortality rate was noted to be considerably higher in the Malaysian hospitals. Antimicrobials, antiepileptics and allopurinol continue to be the major causes of SCARs in Malaysia for close to twenty years. We now know that there are specific genetic markers for carbamazepine- and phenytoin-induced SCARs,^{7,8} and that these allelic markers occur with varying frequency in different ethnic

populations. Whether this holds true for the indigenous peoples of the state of Pahang resulting in higher SCAR rates among them requires further pharmacogenomic studies. Antimicrobials being the predominant culprit group in most of the studies above not only

reflects the high infectious diseases burden in tropical and subtropical Asia, but also serves to remind us of more judicious prescriptions of these agents in the future.

Table 1 Rates of SCAR among both Genders and Various Ethnic Groups

	No. of new patients N (%)	No. with SCAR N (%)	SCAR rate (%)
Gender			
Male	3567 (48.5)	11 (44)	0.31
Female	3786 (51.5)	14 (56)	0.39
Ethnicity			
Malay	5697 (77.5)	16 (64)	0.28
Chinese	1176 (16.0)	6 (24)	0.51
Indian	322 (4.4)	2 (8)	0.62
Indigenous	158 (2.1)	1 (4)	0.63
Total	7353	25	0.34

Table 2 Comparison of Clinicoepidemiological studies on SCAR in Malaysia and Various Asian Countries

	Beijing, China N=50 ¹	Johor bahr, Malaysia N=144 ²	Singapore N=42 ³	Klang, Malaysia N=33 ⁴	Thailand N=97 ⁵	Jammu, India N=446	Our study (2013 - 2016) N=25
Male: Female ratio	01:00.9	NA	1:01	1.36:1	01:02.0	1.59:1	01:01.3
Mean age (years)	40.0±20.0	NA	51.8	42.8 (7- 81)	52.7 (17- 97)	(3-65)	53.7 (4-92)
Median latency (days)	7.64±8.32	16-28	10 (1 -36)	13.1	NA	3-5 weeks	10.5
Incidence/ Prevalence (%)	Incidence: 0.16 Prevalence: 18.6	Incidence: 0.34 Prevalence: 39.8	NA	NA	NA	NA	Incidence: 0.34 Prevalence: 40.3
Commonest SCAR (%)	1. SJS (46.0) 2. DRESS (20.0) 3. TEN (12.0)	1. SJS (61.1) 2. DRESS (23.6) 3. TEN (14.6)	1. SJS (54.8) 2. AGEP (24.0) 3. TEN (11.9)	1. SJS (75.8) 2. DRESS (15.1) 3. TEN (9.1)	1. SJS/TEN (42.3) 2. DRESS (40.2) 3. AGEP (17.5)	1. SJS (45.4) 2. DRESS (36.4) 3. TEN (6.8)	1. SJS (60.0) 2. TEN (24.0) 3. DRESS (8.0)
Commonest Groups of Culprit Drugs (%)	1. AMs (58.0) 2. AEDs (22.0) 3. TCM (32.0)	1. AEDs (31.9) 2. Allopurinol (26.4) 3. AMs (24.3)	1. AMs (50.0) 2. Allopurinol (14.3) 3. AEDs (11.9)	1. Allopurinol (33.3) 2. AMs (30.3) 3. AEDs (12.1)	1. AMs (24.7) 2. Allopurinol (21.6) 3. AEDs (19.6)	1. AEDs (59.1) 2. AMs (18.2) 3. NSAIDs (11.4)	1. AMs (44.0) 2. Allopurinol (36.0) 3. Unknown (12.0)
Mortality rate (%)	NA	6.9	2.4	6.1	8.2	4.5	8

I. SJS: Stevens-Johnson Syndrome; DRESS: Drug-Related Eosinophilia With Systemic Symptoms; TEN: Toxic Epidermal Necrolysis; AEDs: Anti-Epileptic Drugs; TCM: Traditional and Complementary Medicine; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; AMs: Antimicrobials; NA: Not Available

II. Incidence: refers to confirmed SCAR among hospitalized patients; prevalence: refers to patients with drug hypersensitivity reactions

Conclusion

SJS was the commonest SCAR encountered in our center. The commonest culprit drug was allopurinol while antimicrobials as a group caused the most SCARs. Indigenous peoples had the highest SCAR rate.

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Conflict of interest

The author declares no conflict of interest.

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