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CASE REPORT

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Characteristics of lupus patients admitted to a major rheumatology center in Malaysia

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Abstract

Background: *Systemic lupus erythematosus (SLE) admission can cause considerable morbidity, mortality and healthcare utilization. SLE generally develops in younger patients who are in their most productive years. That said, it is pivotal to determine predictors for poor outcomes (disability and mortality) from SLE hospitalization especially among highly developing Asian countries like Malaysia.*

Methods: *Our retrospective cross-sectional study involved adults aged 12 years and above with underlying SLE who were admitted to the medical ward of our hospital between January 2018-December 2018.*

Results: *This study demonstrated that infection and lupus flare are the main causes of hospitalization. Nearly one-fifth (18.9%) of lupus hospitalization had poor outcomes. Multivariate logistic regression analysis revealed that high disease activity (OR=1.15, 95% CI 1.05-1.47, p=0.001) and concurrent flare with infection (OR=1.10, 95% CI 1.02-1.53, p=0.007) at hospitalization were remarkably associated with poor outcome at discharge.*

Conclusion: *Optimization of disease activity and infection control during outpatient's visits is crucial to improve hospitalization outcome.*

Keywords: *systemic lupus erythematosus (SLE), lupus, admission, flare, infection*

Introduction

The systemic lupus erythematosus (SLE)'s admissions varied among countries and regions, partly due to different local clinical practice and different healthcare setting. Admission rates could range from 13.1% in Singapore cohort [1] to 18.9% in North American cohort [2]. However, there was paucity of such data for the past one decade in this regard especially in Asian region like us. This retrospective cross-sectional study was conducted in a major rheumatology referral center from Northern region of Peninsular Malaysia. Pulau Pinang is the most urbanized state and has the highest population density in our country, with 1666.3 every km2 according to 2017 census, with multiethnic composition. All lupus admissions were identified by the attending physicians or rheumatologists and the hospitalization records were retrieved from the discharge summary and case note entered into the computer system in rheumatology unit. Only the first admission was counted throughout the study period. Lupus or mixed connective tissue or overlap syndrome that fulfilled 2012 SLICC criteria [3], were included. Poor outcomes were defined as inability to perform basic self-care activities without help after discharge (dressing, feeding, bathing, grooming and toileting), and including death. Good outcome means no disability after discharge. (Modified from American College of Rheumatology 1991 functional class) [4].

Methods

Data was analyzed using Statistical Product and Service Solutions version 22.0. Multivariate analyses were performed to determine the association between the variables and the outcome. The level of significance was set at 5% (≤0.05).

Results

A total of 122 adults aged 12 years and above were admitted to the medical ward of our hospital with SLE between January 2018-December 2018. The median age of our lupus admission cohort was 39 years old and 91.8% (n=112) were females. In terms of outcome, no differences among gender (p=0.088) or ethnics (p=0.107) (Table 1). Main aetiologies for hospitalization were infection (44.3%, n=54), flare-up of lupus (32.8%, n=40), concurrent flare-up and infection (11.5%, n=14), thromboembolic events (4.9%, n=6) and other reasons (31.1%, n=38). Other reasons were mainly co-managing the lupus patients with other disciplines, for instances, adhesion colic (surgery), induction of labour (obstetrics and gynaecology), major depression (psychiatry), post-fall knee hematoma (orthopaedics). Nearly one-third of infection (27.8%, n=16) arose from patients who were on high dose steroid (more than 7.5 mg daily of prednisolone). About three quarters of infection, 39/53 (73.6%) were either due to cellulitis, pneumonia, urinary tract infection or acute gastroenteritis. The remaining fourteen infection cases included three bacteremia, two dengue infection, two meningoencephalitis, one tuberculosis, one upper respiratory tract infection, one cerebral abscess, one varicella zoster, one necrotizing fasciitis, one infective endocarditis and one cholecystitis. All infection cases did not require intensive care admission, unless it was associated with concurrent flare (31.58% of concurrent flare and infection).

Discussion and conclusion

Lupus flare in our cohort usually involved more than one major organ flares (60% of cases). Neuropsychiatric system and

Table 1: *Demographics and clinical characteristics of lupus patients admitted to our hospital.*

Characteristic	All Patients N = 122 (100%)
Age (in years) Mean ± Standard Deviation	39.00 ± 14.59
Gender, n (%)	
Female	112 (91.80)
Male	10 (8.20)
Ethnicity, n (%)	
Malay	53 (43.40)
Chinese	50 (41.00)
Indian	16 (13.10)
Indonesian	3 (2.50)
Education level, n (%)	
Secondary	93 (76.20)
Tertiary	29 (23.80)
Comorbidities	
None	88 (72.10)
Hypertension	20 (16.40)
Diabetes mellitus	11 (9.00)
Dyslipidemia	10 (8.20)
Chronic kidney disease	4 (3.20)
Gout	2 (1.60)
Duration of lupus (in years)	
Mean ± Standard Deviation	6.85 ± 8.26
Prednisolone dose used, n (%)	
Low dose steroid (less than or equal to 7.5mg daily)	83 (68.00)
High dose steroid (> 7.5mg daily)	39 (32.00)
Immunosuppressants used, n (%)	
None	46 (37.70)
Azathioprine	28 (23.00)
Mycophenolate mofetil	20 (16.40)
Methotrexate	4 (3.30)
Cyclophosphamide	3 (2.50)
Leflunomide	2 (1.60)
Ciclosporin	2 (1.20)
Tacrolimus	2 (1.20)

Table 2: *Multivariate analysis (good outcome = no disability after discharge was taken as reference, 1.00).*

Parameters	Odds Ratio	95% Confidence Interval	p value
Disease activity score (SLAM-R)7 ≥ 7 versus < 7	0.15 (= 85% less likely to be associated with good outcome if the score ≥ 7)	0.05-0.47	0.001
Concurrent flare and infection versus No concurrent flare and infection as reason of admission	0.10 (= 90% less likelihood of getting good outcome if admitted with concurrent flare and infection)	0.02-0.53	0.007

Table 3: *Literature review of selected lupus hospitalization studies.*

Author/ year	Study design/ period	No of subjects/ Origin	Mean Age at admission (years)	Gender	Duration of SLE (years)	Commonest reason of admission	Popular organ(s) in flare	Death	Commonest cause of death
Edwards CJ et al. [1]	Retrospective/ Over 1 year	223/ Singapore	38.4	93% females	7.40	Flare (58%)	Renal (11%)	11 (3.2% of admission)	Infection (82%)
Lee J et al. [2]	Retrospective/ Over 3.5 years	96/ Canada	46.5	91.7% females	13.20	Flare (17.5%)	Renal and Hematological (53%)	9 (5.8% of admission)	Infection (50%)
Ours	Retrospective/ Over 1 year	122/North Malaysia	39.0	91.8% females	6.85	Infection (44.3%)	Renal and Brain (60%)	6 (4.9% of admission)	Infection (50%)

kidney were the two major organs where flare occurred (9/15, 60.0%). Higher percentages (57.1%) of patients with renal or neuropsychiatric flares required longer hospital stays, defined as more than 7 days, compared to those flares without the involvement of these two organs (42.9%). Majority of patients with these two organs' flare had underlying SLE of less than 1 year (10/15, 66.7%), with three of them belonged to the newly diagnosed lupus group. Probable explanations were that they were not adequately exposed to immunosuppressants and steroids. Furthermore, the ability of hydroxychloroquine to prevent flare and protect against organ damage required continuation of hydroxychloroquine for more than one year. Aouhab et al. [5], had observed that patients who have taken hydroxychloroquine for less than a year are more likely to have flares, compared with those who are treated for longer than a year.

In the 6 patients who succumbed, 50% were due to pneumonia and sepsis (unknown source). 1 mortality (16.7%) was due to pulmonary embolism, 1 (16.7%) died of advanced endometrial malignancy and the other one (16.7%) had neuropsychiatric and renal failure. Two thirds of deaths (4/6, 32%) had short SLE duration of below 5 years. Dosage of prednisolone was low (less than 7.5 mg daily). Interestingly, the mortality in our cohort followed bimodal age patterns, i.e., among those aged 21-29 and those aged 46-66. The younger aged group tend to die of infection consistent with the pattern observed by Urowitz et al. [6]. None of them died of atherosclerosis-related vascular events.

Multivariate analysis from our lupus admission cohort revealed that active disease (defined as SLAM-R [7] score ≥7) and concurrent flare with infection as cause of admission were independently associated with poor outcomes (p=0.001 and p=0.007, respectively) (Table 2). Active disease patients were more likely to accrue organ damage as shown by Koelmeyer et al. [8]. Indeed, higher prevalence of organ damage was associated with disability including work disability [9,10].

Apart from that, we observed that those with concurrent lupus flare and active infection had prolonged hospital stays (median stay of 11.5 days versus 6 days or 7 days for those with flare alone or infection alone, respectively) and had higher probability of ICU admissions (31.6% versus 7.7% or 0% if flare alone or infection alone, respectively). Pertinently, concomitant flare and infection posed a great challenge to treatment approach. While increasing steroid potency remained cornerstone of flare control, it might also heighten the risk of mortality from concurrent fulminant infection.

Table 3 showed the comparison between the results of prior studies and ours.

This study highlights that optimal and early lupus intervention remained an unmet need in SLE. Although we are far more advanced in attesting emerging biologics and JAK inhibitor for rheumatoid arthritis and spondyloarthropathy, evidence for SLE as one of our earliest and commonest autoimmune disease are still lacking. Conquering lupus will depend on designing timely and effective pre-hospitalization strategies. These include prelupus intervention and early detection via novel biomarkers as well as individualized treatment approach. The ultimate goal is to achieve remission or at least low disease activity as early as possible to prevent SLE admissions.

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