ORIGINAL ARTICLE

JIACM 2019; 20(3-4): 175-78

Clinical Profile of Lupus Myocarditis-Related Deaths at a Tertiary Care Centre in India

Prabhat Kumar, Gangadharaiah Bharath**, Manish Soneja***, Piyush Ranjan***, Ashustosh Biswas****, Naveet Wig*****

Abstract

***Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease that can have varied clinical manifestations. This study intended to evaluate the clinical profile of lupus myocarditis-related deaths at a tertiary care centre in India over a period of 5 years.*

***Methods:** This was a retrospective study done on SLE patients' admitted under department of medicine of our institute, who had lupus myocarditis-related mortality. The demographic, presenting complaints, duration of SLE, treatment history, clinical parameters, laboratory investigations, SLE related organ involvement, systemic lupus erythematosus disease activity score (SLEDAI) at admission and treatment received during hospital stay were collected from the medical records.*

***Results:** Out of 55 SLE mortalities noted during this period, 12 (21%) patients had lupus myocarditis. The mean age of the patients was 25.1 ± 8.2 years and mean duration of hospital stay was 7.3 ± 6 days. The most common symptom at the time of presentation was dyspnoea, fever and arthralgia (66% each). Hypothyroidism was the most common associated co-morbidity (33%). The mean serum CRP (55.6 ± 41.5 mg/l) and ESR (50.5 ± 28.6 mm/hr) levels were elevated. Serum complement levels were low in 6 (50%) patients and the median SLEDAI score was 18.8 ± 11.6. Lupus nephritis (75%) was the most common associated organ affected in these patients. All patients had global hypokinesia with reduced ejection fraction on echocardiography. Serum Troponin I levels were elevated in 9 (75%) patients. Steroids were the most commonly used treatment in lupus myocarditis patients.*

***Conclusion:** Lupus myocarditis is not so uncommon during SLE flare. It should always be considered in SLE patients with unexplained dyspnoea and tachycardia. Lupus nephritis is commonly associated with lupus myocarditis. Echocardiography and serum cardiac enzymes assist in diagnosing this entity. Lupus myocarditis is usually treated with high dose steroids and other supportive measures.*

***Key words:** Echocardiography, C-reactive protein, lupus nephritis, steroids.*

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease which can affect various organ systems, including heart. The heart is affected in almost 50% of SLE patients and can involve any cardiac structure[1]. Pericarditis is the most common cardiac involvement followed by coronary artery disease, arteritis, valvular heart disease and lupus myocarditis[2]. Lupus myocarditis is a rare manifestation of SLE which is invariably fatal, if not diagnosed and treated promptly[3]. Symptomatic lupus myocarditis has a prevalence of only 5 - 10%, however, autopsy studies have shown a much higher prevalence of 40 - 70%[4]. The rarity of this condition precludes controlled trials and limited data is available from Indian subcontinent. The primary aim of this study was to study the clinical profile of SLE patients who died because of lupus myocarditis at a tertiary care centre in India.

Subjects and Methods

This was a retrospective observational study done in the Department of Medicine at All India Institute of Medical Sciences, New Delhi. The study was approved by the ethics committee of the institute. All death records between January 2014 and January 2019 with diagnosis of lupus myocarditis and satisfying either 1997 American College of Rheumatology Modified Classification Criteria or the 2012 Systemic Lupus International Collaborating Clinics Classification Criteria for diagnosis of SLE were included in the study. Patients having overlap syndrome and death records having insufficient information were excluded from the study. A total of 55 SLE related deaths occurred during this period and 12 (21%) patients had lupus myocarditis. Lupus myocarditis was defined as left ventricular dysfunction on echocardiography in clinically suspected individuals which was attributed to SLE disease activity. Left ventricular dysfunction due to aetiologies

**Assistant Professor, Department of Medicine, ABVIMS and Dr Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, New Delhi -110 001.*

***Junior Resident, ***Associate Professor, ****Professor, Department of Medicine, AIIMS, Ansari Nagar, New Delhi - 110 029.*

Corresponding Author: Dr Prabhat Kumar, Assistant Professor, Department of Medicine, ABVIMS and Dr Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, New Delhi -110 001. Tel: 9968123167, E-mail: drkumar.prabhat@gmail.com.

other than SLE was excluded from the study. The demographic, presenting complaints, duration of SLE, treatment history, clinical parameters, laboratory investigations, SLE related organ involvement, systemic lupus erythematosus disease activity score (SLEDAI) at admission and lupus myocarditis treatment received during hospital stay were collected from medical records on a predesigned proforma.

Statistical analysis

The statistical analysis was performed using Stata 13 software. Continuous variables were expressed as mean and standard deviation (SD) or median and range (if any outliers). Qualitative variables were summarised as frequency and percentage.

Results

Out of 12 patients included in the study, 11 were female and only 1 patient was male. The mean age of the patients was 25.1 ± 8.2 years and mean duration of hospital stay was 7.3 ± 6 days. The median duration of SLE was 1 month (Range: 0 - 60 months) and 5 patients were newly detected cases of SLE (Table I). The most common symptom at the time of presentation was dyspnea, fever and arthralgia (66% each), followed by oral ulcers (50%), cough (41%), seizure (33%), oliguria (33%), photosensitivity (25%), psychosis (25%) and alopecia (25%). Hypothyroidism was the most common associated co-morbidity (33%). None of the patients had hypertension, diabetes, coronary artery disease or antiphospholipid syndrome. Half of the patients were on oral steroid therapy and two patients were receiving mycophenolate at the time of admission.

Table I: Demographic and Clinical features of Lupus myocarditis.

Variables	Mean ± standard deviation
Age	25 ± 8 years
Duration of SLE	10 ± 20 months
Duration of hospital stay	7.3 ± 6 days
SLEDAI score	18.8 ± 11.6

The mean haemoglobin was 9.4 ± 2.1 gm/dl, urea (77.6 ± 55.8 mg/dl), creatinine (1.3 ± 0.9 mg/dl), ESR (50.5 ± 28.6 mm/hr) and CRP (55.6 ± 41.5 mg/l) (Table II). Serum complement levels were low in 6 (50%) patients and the mean SLEDAI score was 18.8 ± 11.6. Lupus nephritis (75%) was the most common associated organ affected, followed by haematological (58%), neuropsychiatric lupus (50%), cutaneous (41%) and myositis (16%) (Table III).

All patients had sinus tachycardia on electrocardiogram. 2 D echocardiography in all 12 patient showed global hypokinesia with left ventricular systolic dysfunction in the form of reduced ejection fraction (< 35%). Pericardial effusion was noted in three patients (25%) and troponin I levels were raised in 9 patients (75%). Steroid was the preferred treatment modality, 9 patients received oral prednisolone (75%) and 8 patient received pulse methyl prednisolone (66%). Intravenous immunoglobulin (IVIG) and mycophenolate (MMF) were given in 3 patients each (25%), whereas only 2 patients received intravenous cyclophosphamide. None of the patients in the present study received either rituximab or plasma exchange (Table IV). Steroids couldn't be administered in few patients either because of early mortality or concomitant infection.

Table II: Laboratory parameters of patients with lupus myocarditis.

Laboratory parameters	Mean ± standard deviation
Haemoglobin (g/dl)	9.4 ± 2.1
Total leucocyte count (cells/cu mm)	7,617 ± 4,538
Platelet count (cells/cu mm)	1,19,916 ± 58,986
Urea (mg/dl)	77.6 ± 55.8
Serum creatinine (mg/dl)	1.3 ± 0.9
AST (U/L)	135 ± 135.8
ALT (U/L)	71.9 ± 60.1
Serum albumin (mg/dl)	2.2 ± 0.3
ESR (mm/hr)	50.5 ± 28.6
CRP (mg/l)	55.6 ± 41.5

AST = Aspartate aminotrasferase, ALT = Alanine aminotransferase, ESR = Erythrocyte sedimentation rate, CRP = C-reactive protein

Table III: Organ systems affected alongwith lupus myocarditis.

Organ involved	Number of patients (%) (n = 12)
Renal	9 (75%)
Haematological	7 (58%)
Serositis	7 (58%)
Central nervous system	6 (50%)
Skin	5 (41%)
Myositis	2 (16%)
Pulmonary	Nil

Table IV: Treatment modalities used in lupus myocarditis.

Treatment modality	Number of patients (%) (n = 12)
Methyl prednisolone pulse	8 (66%)
Oral prednisolone	9 (75%)
Intravenous immunogobulins (IVIg)	3 (25%)
Intravenous cyclophosphamide	2 (16%)
MMF	3 (25%)
Rituximab	Nil
Plasma exchange	Nil

Discussion

This study showed that lupus myocarditis is not an uncommon entity and is one of the leading causes of mortality in SLE patients. The most common symptom of lupus myocarditis in our study was dyspnoea and all patients had unexplained tachycardia. Echocardiography and serum Troponin I levels assisted in diagnosing this entity. Immunosuppression in the form of high dose steroid remains the cornerstone of lupus myocarditis therapy.

Lupus myocarditis, like any other myocarditis can present with dyspnoea, fever, orthopnoea, pedal oedema, palpitations, chest pain or diaphoresis[5]. Dyspnoea and fever was the most common presenting complaint in our study too. Lupus myocarditis is more prevalent in younger age group and in newly diagnosed SLE patients[6]. We also had a similar finding as almost one-third of our patients were newly detected SLE cases. Lupus myocarditis is invariably associated with high disease activity with involvement of other organ systems[7]. Lupus nephritis is the most common organ affected with lupus myocarditis, possibly because of common underlying pathogenesis of immune complex deposition in these two organs[8]. Lupus nephritis was present in 55 per cent patients of LUMINA cohort with myocarditis, whereas in a study by Du Toit *et al*, lupus nephritis was found in almost 68% cases of lupus myocardits[3,6]. In our study 75% patient of lupus myocarditis had associated lupus nephritis. Myocarditis in SLE is also associated with myositis, as evident in our study too[9]. Serum CRP is known marker of disease activity in SLE and lupus myocarditis[10,11]. Our finding of raised serum ESR and CRP levels in lupus myocarditis patients is consistent with earlier studies.

The diagnosis of lupus myocarditis is suspected in patients with features of congestive heart failure or unexplained tachycardia. A number of non-invasive tests help in diagnosing lupus myocarditis, although endomyocardial biopsy remains the gold standard. ECG changes in lupus myocarditis are non-specific and show tachycardia with or without ST changes[12]. Our entire study population had only sinus tachycardia. Cardiac biomarkers like Troponin I is often elevated in these patients suggesting myocardial injury[13]. We found raised Troponin I levels in 75% of our patients. Echocardiography is an easily available tool which assists in diagnosing lupus myocarditis. The finding of global/regional wall motion abnormalities with systolic or diastolic dysfunction, in the absence of other known causes, is highly suggestive of lupus myocarditis[14]. Pericarditis and endocarditis are often associated with lupus myocarditis[15]. Echocardiography suggested severe global hypokinesia with reduced ejection fraction in all our patients and pericarditis was observed in 25% of patients. Treatment of lupus myocarditis includes supportive therapy for heart failure with oral or intravenous steroid therapy. Other immunosuppressant like cyclophosphamide, intravenous immunoglobulins, mycophenolate or rituximab can be also used[16]. Steroids were the most commonly prescribed medication in our study followed by intravenous immunoglobulin. The data regarding mortality in lupus myocarditis is quiet variable with some studies suggesting favourable outcome and few suggesting a higher mortality rate in myocarditis patients[6].

Conclusion

SLE associated myocarditis is commonly associated with high disease activity and lupus nephritis is the most common associated organ involved. Dyspnea and tachycardia is the most common clinical feature of lupus myocarditis. Echocardiography is the most reliable non-invasive tool for the diagnosis of this entity, along with serum cardiac enzymes. High dose steroids remain the drug of choice with other supportive measures. It is pertinent for clinicians to look beyond lupus nephritis in SLE patients.

References

1. Doria A, Iaccarino L, Sarzi-Puttini P. Cardiac involvement in systemic lupus erythematosus. *Lupus* 2005; 14: 683-6.
2. Moder KG, Miller TD, Tazelaar HD. Cardiac involvement in systemic lupus erythematosus. *Mayo Clin Proc* 1999; 74: 275-84.
3. Apte M, Mcgwin G, Vilá LM. Associated factors and impact of myocarditis in patients with SLE from LUMINA, a multiethnic US cohort (LV). [corrected]. *Rheumatology (Oxford)* 2008; 47: 362-7.
4. Sasson Z, Rasooly Y, Chow CW. Impairment of left ventricular diastolic function in systemic lupus erythematosus. *Am J Cardiol* 1992; 69: 1629-34.
5. Cooper LT Jr. Myocarditis. *N Engl J Med* 2009; 360: 1526-38.
6. Du Toit R, Herbst PG, van Rensburg A. Clinical features and outcome of lupus myocarditis in the Western Cape, South Africa. *Lupus* 2017; 26: 38-47.
7. Law WG, Thong BY, Lian TY. Acute lupus myocarditis: clinical

features and outcome of an oriental case series. *Lupus* 2005; 14: 827-31.

8. Bidani AK, Roberts JL, Schwartz MM. Immunopathology of cardiac lesions in fatal systemic lupus erythematosus. *Am J Med* 1980; 69: 849-58.
9. Borenstein DG, Fye WB, Arnett FC. The myocarditis of systemic lupus erythematosus: association with myositis. *Ann Intern Med* 1978; 89: 619-24.
10. Williams RC Jr, Harmon ME, Burlingame R. Studies of serum C-reactive protein in systemic lupus erythematosus. *J Rheumatol* 2005; 32: 454-61.
11. Zawadowski G, Klarich K, Moder K. A contemporary case series of lupus myocarditis. *Lupus* 2012; 21: 1378-84.
12. Morgera T, Lenarda AD, Dreas L. Electrocardiography of myocarditis revisited: Clinical and prognostic significance of electrocardiographic changes. *Am Heart J* 1992; 124: 455-67.
13. Smith SC, Ladenson JH, Mason JW. Elevations of cardiac troponin I associated with myocarditis: Experimental and clinical correlates. *Circulation* 1997; 95: 163-8.
14. Pinamonti B, Alberti E, Cigalotto C. Echocardiographic findings in myocarditis. *Am J Cardiol* 1988; 62: 285-91.
15. Bulkley BH, Roberts WC. The heart in systemic lupus Erythematosus and the changes induced in it by corticosteroid therapy. A studyof 36 necropsy patients. *Am J Med* 1975; 58: 243-64.
16. Appenzeller S, Pineau CA, Clarke AE. Acute lupus myocarditis: Clinical features and outcome. *Lupus* 2011; 20: 981-8.