BJ
BANTAO Journal

BANTAO Journal 2007; 5 (2) : 65–69

Original Article

Lupus Nephritis and Cardiovascular Disorders - Our Clinical Expirience

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Abstract

Background. The aim of this study was to evaluate most common cardiovascular complications in our LN pts.
Methods. We investigated 44 LN pts with cardiac manifestation to conclude which of these are more frequent. In order to achieve the aim of this study, we carried out noninvasive cardiac procedures including measurement of biochemical markers of cardiac function, electrocardiography, echocardiography, computer tomography and magnetic resonance imaging of the heart as well as invasive coronarography in some patients.
Results. Some forms of pericarditis were found in 39/44 pts, substantial pericardial effusion in 3, and 18 pts with pericarditis sicca. Except pericarditis, we identified Libman-Sacks verrucous endocarditis in 3 pts, then other non-specific valvular involvement such as prolapsus with some degree of regurgitation in 27 patients and thickening or degenerative dysfunction in 14 cases. Occurrence of thrombosis in the coronary arteries and the heart valve as well as intramyocardial vasculopathy in the form of the secondary anti-phospholipid syndrome was reported in 8 patients. Myocardial infarction developed due to inflammatory changes in coronary arteries (coronaritis) was identified in one of those patients. Tachycardia is the most common rhythm irregularity but, we found cardiac conduction defects during myocarditis in 6 pts who were also indicated for the therapy due to the metabolic and electrolyte dysbalance.
Concluson. The most common cardiac disorders caused by LN which were detected in our group of patients were forms of pericarditis, valvular thickening and regurgitation while the classic endocarditis or myocarditis was found to be rare.

Keywords: Lupus nephritis, complications, pericarditis, endocarditis, tachycardia

Introduction

Sistemic lupus erithemathodes (SLE) is a syndrome with multifactorial etiology characterized by inflammation affecting almost all or a part the human body. Fifty years ago, mortality rate was 50% but, nowadays, it is assessed that, by careful monitoring of this disease, the 10-year survival period is 90% [1-4]. Once the disease affects the kidneys, we are dealing with lupus nephritis (LN) which is by itself considered a clinical entity. The deterioration of the general condition of the body affects the cardiovascular system as well. The neuroendocrine system collects and processes the information from the internal environment and external surroundings and transmits the responses back to all the organs, tissues and systems. The response thus processed at the level of cardiovascular system leads to normal, faster or slower heart beating, to narrowing or weakening of the vascular system accompanied by an increase or decrease in the arterial pressure to the possible various paradoxical reactions in tissues and organs. As the genesis of the cardiovascular diseases is not uniform, the manifestation of the same is neither uniform nor predictable.
The main morphologic lesion in SLE is diffuse microvasculitis and the cardiac involvement in various forms is found during the autopsy [5-7]. But the development of cardiovascular complications is less perceived and very often concealed by symptoms and signs indicating involvement of other organs, particularly, the kidneys. While there has been some improvement in the SLE survival pattern achieved by the immunosuppressive therapy [7,8] the recent studies indicate the significance of cardiovascular diseases as the most serious cause of death [9-13].
Pathophysiologically, SLE is characterized by pancarditis affecting the pericardium, myocardium, endocardium and coronary arteries. In the autopsy findings, pericarditis was reported in 43% out of 100% of cases (in 62% on average), myocarditis in 8% out of 78% of cases (in 40% on average), but they usually were not diagnosed clinically. Libman-Sacks lesions were detected in 25% out of 100% of cases (in 43% on average) while infectious endocarditis was identified in 1,1% - 4,9% of clinical autopsies [11]. The coronary disease results from arteritis and may be pharmacologically or surgically treated. In cases of the heart valve defects, surgical treatment is applied but surgical mortality rate in SLE is 25% higher. Aortic insufficiency and mitral regurgitation are considered the most common valvular defects, although aortic and mitral valve stenosis is included. Hypertension was reported in 14-69 %, while the heart failure in 5-55% of cases [11-13]. What left to be done is to assess to what extent the improved diagnosis and the treatment of the SLE cardiovascular manifestations would improve the survival pattern in those patients.
Having in mind everything mentioned so far, there is a great amount of research work to be done with respect to the genesis, pathomorphology and, clinical but also casual manifestations of the cardiovascular system in lupus nephritis. Our experience in treating cardiac complications in 44 cases was presented in this study.
The aim of our study was to determine the frequency of clinical cardiovascular disorders in patients with lupus

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nephritis and their eventual significance for the follow-up monitoring, treatment and prognosis as well.

Patients and methods

Direct or indirect signs of cardiovascular abnormalities were seen in 51 out of 92 reported SLE patients treated at the Military Medical Academy in the period from 1986 to 2006. Lupus nephritis was diagnosed in 44 out of 58 patients with SLE and cardiovascular manifestations. Data were gathered retrospectively from both the existing database of patients examined and treated on an inpatient basis and, the database of patients ambulatory monitored. In dealing with these patients, a multidisciplinary approach was used. All the patients were adequately treated and observed for the period of 4 years. According to the objectives established in this study, the involvement of the cardiovascular system was determined on the basis of noninvasive and invasive cardiac diagnostic methods while the clinical studies were the base for determining other cardiovascular disorders. The data gathered from all non-invasive cardiovascular procedures including measurement of biochemical specific markers of the heart function such as cardiospecific enzymes, troponin, brain natriuretic peptide-BNP, electrocardiography, echocardiography, computer tomography and magnetic resonance of the heart as well as from invasive coronarography performed in some patients were thoroughly assessed. The cause of death was established on the basis of clinical or autopsy reports.

Results

Patient outcome: Out of 44 patients 39 were female and 5 male patients. The average age was 33,2 (Table 1). During the 4-year observation period, 28 patients maintained a good health condition and 16 died (12 from cardiac causes, 1 from a non-cardiac cause while for the last 3 patients we had no information).

Table 1. Heart function in patients with Lupus nephritis and cardiovascular disturbances estimated by echocardiografic ejection fraction

Functional state of heart by echocardiografic ejection fruction in our patients			
General aspects	X		SD
Number of patients		44	
Male/female		39/5	
Age (years)	33,2		±17,11
Ejection fraction of heart	53,43		±9,37%

We estimated cardiac condition of all our patients by appropiate diagnostic procedures (Table 2). Only in 2 out of 44 patients there were not clinical, but positive diagnostic results for cardiac disturbances.

Table 2. Assessment of clinical state by different diagnostic procedures

Presence of cardiac clinical manifestation and diagnostic approach in patients with Lupus nephritis					
Examination	**Out of 44 pts**	**STATUS**	**PTS NUMBER**	**PERCENT**	
Clinical presentation	44	positive	42	42/44	95
	(100%)	negative	2		
Resting ECG	32	normal	32	12/32	37
	(73%)	abnormal	12		
Ambulatory ECG (Holter)	6	normal	2	4/6	66
	(13%)	abnormal	4		
Echocardyography	44	normal	13	31/44	70
(TTE,TOE)	(100%)	abnormal	31		
CT / MRI	8	normal	4	4/8	80
	(18%)	abnormal	4		
Cardiac catheterisation	3	normal	0	3/3	100
	(7%)	abnormal	3		
Coronary angiography	2	normal	0	2/2	100
	(4%)	abnormal	2		
Cardiospecific enzyme	19	normal	7	12/19	63
	(43%)	abnormal	12		

TTE - transthoracic echo, TOE - transoeseophageal echo, CT - computer tomography, MRI - magnetic resonance imaging

Among the general clinical manifestations characteristic for dysfunction of the heart, the following were identified (Table 3).

Abnormalities in normal rhythmic pattern out of which tachycardia is the most common manifestation reported in 33/34 cases.

Cardiac conduction defect is more severe form of disorder of the normal heart function and is usually associated with myocarditis. The more severe abnormalities were detected in 6 patients while one was indicated for the insertion of an artificial pacemaker due to high atrioventricular blocking of the II degree.

Valvular defects: Valvular defects were reported in 29 patients. Echocardiographically recorded morphologic changes in the form of Libman-Sacks endocarditis were identified in 3 patients. The most frequently reported defect was non-specific thickening of valves (in 27/29 patients). Thickening of valves free of any signs of endocarditis was seen in 14 patients with mitral valve prolapse. Haemodynamically substantial damage of valvular structures wasn't found in any of those patients.

Table 3. Presents of different cardiac conditions and cardiac state in our group of patients with Lupus nephritis and cardiac disorders

Cardiac conditions	Out of 44 pts	Clinical status	N of patients	%
Rhythm and conduction disturbances	34 (77%)	Tachycardia	33/34	97
		Arrythmias	11/34	32
		Conduction defect	6/34	17,6
Valvular defects	29 (66%)	Thickening of valve	27/29	93
		Prolapsus	14/29	48,2
		LS-endocarditis	3/29	10,3
Pericarditis	27 (61%)	Pericarditis sicca	18/27	66,6
		Pericardial effusion	9/27	33,3
		Cardiac tamponade	1/27	3,7
Myocarditis	4 (9%)	Myocardiopatia	4/4	
Cardiomiopathy	4 (9%)	Heart failure	4/4	
IHD and trombosis	3 (7%)	Coronary sindroma	2/3	

PTS-patients, CVD-cardiovascular disease, IHD-ishaemic heart disease

Pericarditis: 39 patients complained of the chest pains and /or dyspnea what was believed to result from the affection of pericarditis associated with the disease activity during the initial examination of the patient or relapsing period as it was seen in 13 patients. The definite diagnosis couldn't be established due to the serologic tests being initially seronegative. But the successive serologic tests found to be seropositive in a certain number of patients revealed other characteristic signs typical for lupus nephritis. Pericarditis was diagnosed in 27 patients. Substantial pericardial effusion was detected in 3 of those 27 pts and a form of pericarditis sicca identified in 18 pts. In 2 cases, the diagnostic punction of pericardium was performed as well as a biopsy to exclude tuberculosis or some other causes of pericarditis. All the patients receiving steroide therapy responded quite well to it.

Myocarditis: Endomyocardial biopsy wasn't performed to diagnose the myocarditis. But in 4 patients that diagnosis was established on the basis of electrocardiograpic changes, echocardiography and serologic tests. The mentioned patients responded promptly to the steroid therapy while azathioprine was introduced into the therapy of one patient.

Pulmonary hypertension: The progressive dyspnea accompanied by generalized edema at the time when the disease was well controlled with steroids was disclosed in two cases. The diagnosis of primary pulmonary hypertension was established by catherisation of the heart and the pulmonary angiography. One of those two patients wasn't in the evidence any more while the other one died from the heart failure.

Cardiomyopathy and coronary artery disease: One patient with clinical manifestations of the chest pains and characteristic electrocardiographic changes was diagnosed as having the acute myocardial infarction developed while the disease was in remission and treated with steroids. That patient wasn't in the evidence any more.

By applying the mentioned diagnostic methods and by using computed tomography and magnetic resonance imaging as well, substantial cardiomyopathy was identified in 4 patients. Three of them died while the fourth was not in the evidence any more. In one of those who died, focal myocardial necrosis and fibrous scar accompanied by intramural stenosis of coronary arteries was found.

Discussion

Cardiovascular disorders in SLE may be a part of clinical manifestations but may considerably be involved in the occurrence of complications associated with the affection of other organs or systems particularly if it's the case of renal failure in LN. However, it may be considered that cardiovascular defects, either relating to functional or diagnosed morphologically organic defects, may substantially affect the further course of disease and its prognosis [5]. The most common forms of the cardiovascular diseases are pericarditis, valvular degeneration such as valvular thickening and regurgitation, while classic endocarditis and myocarditis were rarely seen [6]. In the early stage of the disease, the acute myocardial infarction may develop due to the inflammatory changes in the coronary arteries (coronaritis), particularly, in young women. Our study indicated that the clinical pericarditis was the most common cardiac complication occurring in LN. Lupus pericarditis is the most often associated with the disease activity. It is known that infectious causes of pericarditis might occur in patients in remission. Treatment with steroids and immunosuppressive drugs may create the opportunity for the development of opportunistic infections but, it may also mask their signs. Therefore, it is proposed to have the pericardium aspirant carefully analyzed each time, taking into account the culture analysis [13]. The diagnostic punction of the pericardium was performed in patients with effusion, but the constrictive pericarditis was detected in patients after the long evolution of the disease. As pericarditis, myocarditis is also associated with the disease activity and responds well to the steroid therapy [12]. The most significant results of the latest studies on SLE and LN indicate the increase in number of patients with changes in coronary blood vessels thought to be the underlying causes of mortality [14-17].

Pulmonary hypertension may also be associated with LN, but cases described in the literature are isolated [8-10]. On the basis of autopsy findings, it was determined that vasculitis affecting the pulmonary vasculature occured more often than it was clinically identified [9,10].

Abnormalities in normal rhythmic pattern may occur regardless of the stadium of the underlying disease. Sinus tachycardia is the most common manifestation of the cardiovascular system. The mentioned disorders reflecting either organic or functional defects are reported.

Contrary to rhythm irregularity, cardiac conduction defects are most often the result of the existing myocarditis and usually develop due to metabolic and electrolyte dysbalance but may also be caused by the already introduced pharmacotherapy including antimalarial drugs particularly [14,15].

The changed lipid status, a high index of the disease activity, the existence of other diseases (hypertension, renal failure,) premature menopause and partially the 'lupus factor' including chronic inflammation, anti-phospholipid antibodies as well as chronic treatment with steroids [14-17] are involved in the genesis of systemic changes in coronary vessels in SLE and LN.

The development of acute myocardial infarction in one relatively young female patient was attributed to the anti-phospholipid syndrome and vasculitis related changes in coronary blood vessels.

Prognosis of cardiomyopathy is, due to the simple or complex cardiovascular changes bad in those patients and the developed disease usually results in cardial death.

Primary cardiomyopathy is reported in a very small number of patients while the secondary often results from either valvular defects or myocarditis [18].

There are no precise information in the literature on the correlation that may exist between the occurrence of cardiovascular diseases and the presence of dsDNA, on the concentration of complements and the presence of aCL antibodies.

Biological survival pattern indicates that cardiovascular diseases are the underlying cause of mortality in the patients with the long-lasting evolution of lupus [19]. Cardiac manifestations inevitably led to the lethal outcome before. It happened that they were diagnosed only during the autopsy. Recently, cardiovascular manifestations are often mild or even asymptomatic. The use of echocardiography and other sophisticated and noninvasive diagnostic methods allows us to identify abnormalities of the heart, particularly mild forms of pericarditis, valvular defects or other forms of myocardial dysfunction, in a large number of cases. Timely diagnosis and the treatment of cardiovascular diseases may prevent certain undesirable effects and play a great part in the successful treatment of the disease. Therefore, a periodical echocardiography is highly recommended in the SLE patients.

Conclusion

Our study shown that cardiovascular complications were substantially present in the SLE and LN patients. The most common were pericarditis, valvular defects such as thickening of valvular apparatus and regurgitation, while the classic endocarditis and myocarditis were found to be more rare.

Treatment of the SLE patients requires, due to the high incidence of cardiovascular diseases in SLE and /or LN patients, a wide range of clinical and laboratory analyses that should serve as the valid standards of SLE and cardiovascular diseases treatment. Periodical examinations of the cardiovascular system by noninvasive techniques are required, even if no visible symptoms of the affection are observed.

It is necessary to conduct further studies as to confirm our observation and, if possible, to set the optimal treatment regimen.

Conflict of interest statement. None declared.

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