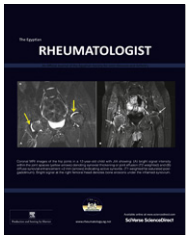
The Egyptian Rheumatologist (2012) **34**, 51–57

Egyptian Society for Joint Diseases and Arthritis

The Egyptian Rheumatologist

www.rheumatology.eg.net
www.sciencedirect.com



ORIGINAL ARTICLE

Comparative study of kidney affection in SLE patients with and without antiphospholipid syndrome

Wafaa Gaber [a,*], Safaa Sayed [a], Yasser Ezzat [b], Tamer Wahid Kassem [c], Haytham Khalil [d]

[a] *Rheumatology and Rehabilitation Department, Faculty of Medicine, Cairo University, Egypt*
[b] *Rheumatology and Rehabilitation Department, Fayoum University, Egypt*
[c] *Radiology Department, Faculty of Medicine, Cairo University, Egypt*
[d] *Clinical Oncology and Nuclear Medicine Department, Cairo University, Egypt*

Received 15 January 2012; accepted 16 January 2012
Available online 2 March 2012

KEYWORDS

Renal DMSA;
Renal MRA;
APS nephropathy;
Systemic lupus erythematosus

Abstract *Aim of the work:* To evaluate the incidence, clinical associations and outcome of APS nephropathy in SLE patients with 2ry APS.

Patients and methods: We studied 64 female SLE patients with nephritis; 32 of them had 2ry APS (group 1) and the rest without 2ry APS (group 2). Demographic, clinical and serological data were prospectively evaluated. Systemic lupus erythematosus disease activity index (SLEDAI) and Systemic Lupus International Collaboration Clinics/ACR damage index (SLICC) were assessed. Renal duplex, renal ^{99m}Tc-dimercaptosuccinic) scan (DMSA scan) and renal magnetic resonance angiography (MRA) were all used to detect renal vascular affection.

Results: There were statistically significant differences between the two examined groups regarding damage index ($p = 0.000$), hypertension ($p = 0.02$), thrombocytopenia ($p = 0.000$), ↓LDL ($p = 0.008$), ↓C3 ($p = 0.01$) and TMA ($p = 0.04$). In group 1: MR angiography detected 7 patients with RAS: 5 patients with renal artery thrombosis that showed a significant association with TMA and proteinuria ($p = 0.002$, $p = 0.004$: $p < 0.001$, $p = 0.02$, respectively). Patients with RAS had ↑DBP, ↑s.creatinine and ↑TGs ($p = 0.004$, $p = 0.005$ and $p = 0.0003$, respectively). Renal DMSA

* Corresponding author. Tel.: +20 01227626502.
E-mail address: wafaagaber3@yahoo.com (W. Gaber).

Peer review under responsibility of Egyptian Society for Joint Diseases and Arthritis.
doi:10.1016/j.ejr.2012.01.001

detected 6 patients with cortical scar which showed a significant association with TMA, proteinuria, livedoreticularis and arthritis ($p = 0.001$, $p = 0.01$, $p = 0.04$ and $p = 0.03$, respectively) those patients had ↑DBP and ↑RI ($p = 0.000$ and $p = 0.006$, respectively).

Conclusion: aPL testing should become a routine investigation in patients evaluated for RAS or renal infarctions especially with hypertension and unexplainable deteriorating renal function. To confirm our results we propose that larger scale, multicentre studies with longer evaluation periods.

1. Introduction

Antiphospholipid antibodies (aPL) are a heterogeneous group of antibodies directed against negatively-charged phospholipids, phospholipid-binding proteins, and phospholipid–protein complexes. The laboratory investigations of the update criteria for definite antiphospholipid syndrome (APS) includes the lupus anticoagulant (LAC), the anticardiolipin antibody (aCL), and the anti-β2 glycoprotein I (β2GPI) antibody [1].

Conley and Hartman initially described the presence of lupus anticoagulants in SLE patients in 1952 [2]. Subsequently, Bowie and his colleagues described thrombosis occurring in patients with circulating anticoagulants in a seminal paper in 1963 [3]. These observations of the association of APA with glomerular and arterial thrombosis in SLE were extended over the next two decades by Kant and his associates, who reported a strong association between the presence of lupus anticoagulants and the presence of glomerular thrombi in renal biopsy specimens systematically performed in SLE patients seropositive for lupus anticoagulant [4]. While the precise origin of APAs in SLE was unclear, their presence appears to consistently correlate with the occurrence of renal thrombotic microangiopathy (TMA).

In the course of the antiphospholipid syndrome (APS), the existence of vaso-occlusive lesions capable of affecting numerous organs is now well established. The renal involvement attributable to APS nephropathy (APSN), corresponds to vaso-occlusive lesions of the intrarenal vessels, associating side-by-side with acute thromboses (with chronic arterial and arteriolar lesions) leading to zones of cortical ischemic atrophy [5].

The renal involvement had been associated with both primary and secondary APS. Clinical features include hypertension, renal artery stenosis, thrombotic microangiopathy and other histological manifestations of the nephropathy (APSN), renal vein thrombosis, APSN in the course of systemic lupus erythematosus and renal failure. APSN is an independent risk factor that should be included in the classification criteria for definite APS with characteristic clinical and histological features [6].

2. Patients and methods

2.1. Patients

Sixty-four female SLE patients fulfilling the updated American College of Rheumatology (ACR) revised criteria for the classification of SLE [7] were consecutively recruited from Rheumatology department, Cairo and Fayoum University hospitals. All of them have nephritis and thirty-two of them have secondary antiphospholipid syndrome. APS was diagnosed according to the Sapporo criteria [8]. Patients are classified into two groups: (group 1) SLE patients with 2ry APS and (group 2) SLE patients without APS. In (group 1) 15/32(46.9%) had recurrent fetal loss, 4/32 (12.5%) had CVA, one patient (3.1%) had Pulmonary artery embolism, also one patient had transverse myelitis (3.1%) and finally 17/32(53.1%) had venous thrombosis. Full history taking, thorough clinical examination and laboratory investigations were done. Assessment of disease activity was performed using the systemic lupus erythematosus disease activity index (SLEDAI) [9], disease damage using the Systemic Lupus International Collaboration Clinics/ACR damage index (SLICC/DI) [10]. Renal biopsy was done to all patients, the specimens processed for light microscopy and classified according to the 1982 modified WHO morphologic classification of lupus nephritis [11]. Informed consents were taken from the patients and the study was approved by the local ethics committee.

2.2. Renal biopsy

The kidney biopsy was performed in all patients who had either proteinuria (urinary protein concentration $\geqslant$ 500 mg/dl), abnormal urinary sediment, or an elevated serum creatinine level. The biopsy specimens had been studied, using light and immunofluorescence microscopy, by renal pathologist who had no knowledge of the clinical and laboratory features of the patients. The World Health Organization (WHO) classification of lupus glomerulonephritis [11] and the WHO activity and chronicity index scores [12] were reevaluated.

The immunofluorescence microscopy findings as described in the initial reports of the kidney biopsies were accepted. APS nephropathy was diagnosed when at least 1 of the following lesions was detected: thrombotic microangiopathy (TMA), characterized by the presence of fibrin thrombi in arterioles and/or glomeruli (acute lesion), or myofibroblastic intimal cellular proliferation leading to intimal thickening of interlobular arteries, organized thrombi with or without recanalization, fibrous arterial and arteriolar occlusion, and subcapsular zone with FCA (chronic lesions) [5] .

2.3. Laboratory investigations

Antinuclear and anti-DNA antibodies, C3, and C4 were assessed according to standard methods. Determination of IgG and IgM antibodies to aCL was performed with an enzyme-linked immunosorbent assay [13], Cardiolipin (50 μg/ml) in ethanol (Sigma, St. Louis, MO) was used as antigen on polystyrene micro titer plates (Nunc, Naperville, IL), which were left to dry overnight at 4 °C. After washing with phosphate buffered saline, the nonspecific binding sites were blocked by

10% bovine serum in phosphate buffered saline. LAC was assayed by activated thromboplastin time [14]. The detection of LAC in medium or high titers of aCL at least 2 times, 6 weeks apart, before or at the time of kidney biopsy, was required [8].

2.4. Exclusion criteria

The criteria for exclusion from the study were other potential causes for renal microangiopathy, such as systemic sclerosis, malignant hypertension, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, postpartum renal failure, preeclampsia, diabetic nephropathy, chemotherapy, or cyclosporine therapy.

2.5. Radiological examination

2.5.1. Renal ultrasound and color Doppler examination

Renal Doppler US was performed successfully in each study patient and was accomplished in 15 min or less. In each patient, both kidneys were examined with real-time US, performed with a 3.5–5 MHz transducer.

Assessment of the size, parenchymal thickness and cortical contour of both kidneys were performed. The echogenicity and cortico-medullary differentiation of the kidneys were assessed.

The intra-renal arteries were examined with pulsed Doppler US at the same respective scanning frequencies. Multiple Doppler signal tracings and a standard gray-scale examination of the kidney were recorded. Doppler signals were, in general, obtained from arcuate arteries at the cortico-medullary junction, interlobar arteries along the border of medullary pyramids, or both. The Doppler waveforms were made on the lowest pulse repetition frequency possible without aliasing. This maximized the size of the Doppler spectrum and decreased the percentage of error in the measurements. In addition, the lowest possible wall filter for each US scanner was used. Doppler sample width was set at 2–5 mm. The resistive index (RI) ([peak systolic frequency shift-minimum diastolic frequency shift]/peak systolic frequency shift) was calculated. The RI for each kidney was calculated as an average value obtained from three to five waveforms recorded in three different regions of the kidney. An RI of $\geqslant 0.70$ was considered abnormal.

The main renal arteries were also examined for focal areas of stenosis or luminal reduction. Multiple Doppler tracings were recorded for elevated peak systolic velocity (PSV) or RI [15].

2.5.2. Magnetic resonance angiography of both renal arteries

All MR angiography examinations were performed by using a 1.5-T whole-body MR system (Philips Medical Systems) with a gradient strength of 30 mT/m and a slew rate of 150 (mT-m-1)/msec. A four-element phased-array body coil was used for signal reception.

Coronal single-shot fast SE or half-Fourier single-shot turbo SE imaging with the following parameters: repetition time (msec)/echo time (msec), ∞/120; flip angle. 90°; and acquisition time, 20 s (breath hold). This heavily T2-weighted sequence provides an overview of the upper abdominal anatomy, renal parenchyma and collecting system and serves as a localizing sequence for planning other sequences in the protocol.

Furthermore, a two-dimensional non enhanced phase-contrast (PC) sequence (5/3 and 50° flip angle) was performed followed by standard time of flight (TOP) sequence (4.2/1.8 and 70° flip angle) [16].

2.5.3. 99mTc-DMSA (^{99m}Tc-dimercaptosuccinic) scan acquisition and interpretation

DMSA scan was performed using a standard protocol. Injected activities were the recommended adult dose in the range of 3–5 mCi (110 MBq–185 MBq). Data were acquired on a dual-head, large-field-of-view gamma camera (Axis-Phillips-Marconi medical systems) equipped with low-energy, high-resolution parallel collimators in a 256×256 matrix. Planar posterior, anterior, left posterior, and right posterior oblique views were obtained 3–4 h after intravenous injection of ^{99m}Tc-DMSA (Renocis; CIS Bio International, Gif-sur-Yvette, France). Acquisitions were continued to a total of 750 kilocounts or 300 s (5 min). No sedation was used [17,18].

Two experienced physicians unaware of the patient's clinical and radiological data interpreted the findings according to the criteria of Patel and his colleagues as shown in (Table 1) and discrepancies were resolved by consensus. At the time of diagnosis, DMSA findings were judged to be abnormal when the criteria for scarring were satisfied. Defects located centrally over the pelvicalyceal system were not considered abnormal [19].

Statistical analysis: The data were coded and entered using the statistical package SPSS version 15. The data were summarized using descriptive statistics: mean, standard deviation, minimal and maximum values for quantitative variables and number and percentage for qualitative values. Statistical differences between groups were tested using Chi Square test for qualitative variables, independent sample *t* test for quantitative normally distributed variables while Nonparametric Mann Whitney test was used for quantitative variables which are not normally distributed. *P*-values less than or equal to 0.05 were considered statistically significant [20].

Table 1 DMSA scan interpretation criteria are according to Patel and his associates [19].

DMSA
Normal findings
• Normal contour: smooth and continuous without indentations
• Homogeneous parenchymal uptake in all regions of both kidneys
• Normal size and shape of both kidneys
Inflammation
• Slightly bulging or normal contour
• Single or multiple, local or diffuse areas of decreased activity in parenchyma which are diffuse or, rarely, spheric, in at least 2 projections
• Mild to severe degree of photopenia or, rarely, complete absence of activity
• No volume loss
Scarring
• Diffuse or sharp indentation in contour with thinning of cortex
• Any shape defects with loss of renal volume
• Photopenia (usually severe) or absent activity

3. Results

3.1. Data of all studied SLE patients (with and without 2ry APS)

There were 64 SLE patients with nephritis, 32/64 (50%) of them had 2ry APS (group 1) and another 32/64 (50%) matched SLE patients with nephritis, but with out 2ry APS as a control group (group 2). The demographic and clinical features are presented in Table 2, laboratory parameters and renal biopsy of the two groups are presented in Table 3 and medication received are presented in Table 4.

3.2. Results of magnetic resonance angiography of both renal arteries

MR angiography had detected 7(21.9%) patients with RAS in (group1) and on comparing the two groups it showed a statistically highly significant difference ($p = 0.005$). RAS appeared as smooth, well-defined and noncritical stenosis distal to the renal artery ostium as shown in (Fig. 1). Patients with RAS showed a significant association with TMA and proteinuria ($p = 0.002$ and $p = 0.004$, respectively). Patients with RAS had higher DBP, s.creatinine, TGs and renal RI than those without RAS ($p = 0.004$, $p = 0.005$, $p = 0.003$ and $p = 0.008$, respectively).

MR angiography also detected 5(15.6%) patients with renal artery thrombosis in (group1) as shown in (Fig. 1) that showed a statistically significant difference ($p0.02$) on comparing the two groups. Patients with renal artery thrombosis showed a significant association with TMA, proteinuria and arthritis ($p < 0.001$, $p = 0.02$ and $p = 0.03$, respectively). Patients with renal artery thrombosis had higher SBP, DBP, thrombocytopenia, s.creatinine, TGs and renal RI ($p = 0.004$, $p = 0.000$, $p = 0.04$, $p = 0.0004$, $p = 0.009$ and $p = 0.04$, respectively).

3.3. Results of ^{99m}Tc-DMSA scan

Renal DMSA scan had detected 6(18.8%) patients with cortical scar as shown in (Fig. 2) which showed a statistically significant difference ($p = 0.02$) on comparing the two groups. It showed also a significant association with TMA ($p = 0.001$) and significant association with proteinuria, livedoreticularis and arthritis ($p = 0.01$, $p = 0.04$ and $p = 0.03$, respectively). Patients with cortical scar had higher DBP and renal RI ($p = 0.000$ and $p = 0.006$, respectively).

3.4. Results of renal ultrasound and color Doppler examination

Renal Duplex detected 12(37.5%) patients with increased echogenecity (nephropathy) which showed a significant association with alopecia, fever, TMA, proteinuria, casturia and mucosal ulcers ($p < 0.001$, $p = 0.02$, $p = 0.005$, $p = 0.004$, $p = 0.02$ and $p = 0.01$, respectively). Patients with ↑ ecchogenecity had higher DBP, renal RI and ESR ($p = 0.02$, $p = 0.000$ and $p = 0.01$, respectively).

Decreased renal size had been detected by renal Duplex in one patient only (3.1%) and showed a significant association with TMA ($p = 0.02$).

4. Discussion

The antiphospholipid antibody syndrome (APS) described a clinical entity with recurrent thrombosis, fetal loss, thrombocytopenia in the presence of lupus anticoagulant and/or antibodies to cardiolipin. These antibodies may be associated with connective tissue diseases such as systemic lupus erythe-

Table 2 Descriptive data of the studied patients.

Demographic features (mean ± SD)	Group 1 (SLE with 2ry APS)		Group 2 (SLE without 2ry APS)		*P* value
Age (years)	29.3	±7.3	25.9	±7.8	0.08
Disease duration (years)	4.9	±3.01	3.1	±2.2	0.02*
Disease Activity & Damage index					
SLEDAI	19.0	±9.04	25.03	±7.7	0.003**
SLICC	1.4	±1.04	0.2	±0.4	0.000**
Clinical Manifestations Number (%)					
Constitutional symptoms	4	12.5%	14	43.8%	0.005**
Mucocutaneous	16	50%	32	100%	0.001**
Arthritis	8	25%	19	59.4%	0.02*
Neuropsychiatric	8	25%	7	21.9%	0.6
Cardiovascular	2	6.3%	0	0%	0.2
Pulmonary hypertension	2	6.3%	2	6.3%	0.2
Vasculitis	6	18.8%	15	46.9%	0.02*
Hypertension	17	53.1%	11	34.4%	0.02*
Miscarriage	15	46.9%	0	0%	0.000**
Venous thrombosis	17	53.1%	0	0%	0.000**
Arterial thrombosis	4	12.5%	0	0%	0.04*
Renal activity index	18	56.3%	26	81.3%	0.03*
Renal chronicity index	17	53.1%	13	40.6%	0.3

SLEDAI: Systemic lupus erythematosus disease activity index. SLICC: Systemic Lupus International Collaborating Clinics.
* is significantly different at $p < 0.05$.
** is significantly different at $p < 0.001$.

Table 3 Laboratory investigations and renal biopsy of the two groups.

Laboratory investigations		Group 1(SLE nephritis with 2ry APS)		Group 2(SLE nephritis without 2ry APS)		*P* value
ESR 1st hour	(mmHg)	37.3	±18.5	45.8	±19.4	0.02*
Hemoglobin	(g%)	10.4	±1.3	10.6	±1.9	0.6
WBCs	($\times 10^3/mm^3$)	4.1	±0.9	4.6	±1.1	0.09
Platelets	($\times 10^3/mm^3$)	118.9	±29.7	209.9	±50.4	0.000**
AST	(U/L)	25.5	±8.7	21.9	±8.7	0.1
ALT	(U/L)	23.3	±9.8	23.7	±8.5	0.8
S.Albumin	(g/dl)	3.3	±0.6	3.1	±0.6	0.3
S.Creatinine	(mg/dl)	1.03	±0.6	0.9	±0.3	0.3
Proteinuria	No (%)	25	78.1%	29	90.6%	0.5
LDL	mg/dl	147.9	±32	171.8	±37	0.008**
HDL	mg/dl	54.2	±16.3	41.8	±11.9	0.001**
Cholesterol	mg/dl	193.3	±61.5	208.3	±80.6	0.5
Triglycerides	mg/dl	157.8	±60.2	197.3	±88.9	0.1
Consumed C3	No (%)	10	31.3%	22	68.8%	0.01*
Consumed C4	No (%)	15	46.9%	17	53.1%	0.3
LAC	No (%)	25	78.1%	1	3.1%	0.000**
ACL	No (%)	31	96.9%	0	0%	0.000**
a-PTT prolongation	No (%)	25	78.1%	1	3.1%	0.000**
Anti-dsDNA	No (%)	14	43.8%	22	68.8%	0.003**
TMA	No (%)	6	18.8%	0	0%	0.04*

ESR: Erythrocyte sedimentation rate, AST: Aspartate transaminase, ALT: Alanine transaminase, ACL: anti-cardiolipin, LAC: lupus anticoagulant, a-PTT: activated partial thromboplastin time ANA: antinuclear antibodies TMA: Thrombotic microangiopathy.
* is significantly different at $p < 0.05$.
** is significantly different at $p < 0.001$.

Table 4 Medications received by the study groups.

Medications	Group 1(SLE with 2ry APS)		Group 2(SLE without 2ry APS)		*P* value
Cumulative steroid dose by gm(mean ± SD)	33.1	±25.5	22.9	±12	0.03*
Cumulative HQN dose by gm(mean ± SD)	440.4	±286.6	378.6	±204.3	0.8
Cumulative azathioprine dose by gm(mean ± SD)	94.7	±97.2	70.7	±58.5	0.7
Cumulative cyclophosphamide dose by gm(mean ± SD)	3.5	±4.03	2.9	±4.1	0.6
Methotrexate No (%)	7	21.9%	6	18.8%	0.8
Marivane No (%)	32	100%	0	0%	<0.001**
Baby aspirin No (%)	26	81.3%	0	0%	<0.001**
Mycophenolate mofetil No (%)	4	12.5%	7	21.9%	0.3

* is significantly different at $p < 0.05$.
** is significantly different at $p < 0.001$.

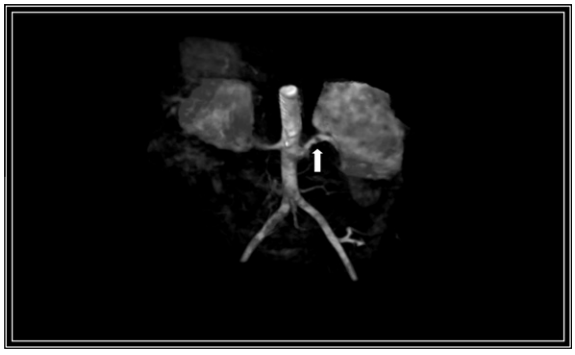


Figure 1 Magnetic resonance angiography shows left renal artery stenosis and thrombosis distal to the renal artery ostium (white arrow).

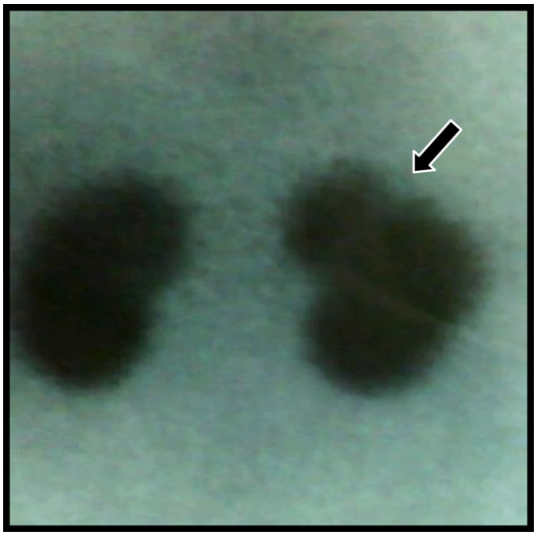


Figure 2 DMSA scan shows small cortical renal infarction (sharp indentation) at upper pole of left kidney (black arrow).

matosus (secondary APS) or be found in isolation (primary APS). Renal syndromes increasingly being reported in association with these antibodies which include thrombotic

microangiopathy, renal vein thrombosis and renal infarction, renal artery stenosis [21].

In the current study we had found that aPL antibodies in SLE patients with renal involvement represent a strong risk factor for the RAS and the thrombotic events within the kidney.

In the present study we had examined 64 SLE patients with nephritis, 50% of them had 2ry APS, to detect renal manifestations caused by aPL antibodies by different means as renal Duplex, renal MRA and renal DMSA scan.

MR angiography detected 7/32(21.9%) patients with RAS, who showed highly significant association with hypertension and this can be explained by the fact that RAS impairs renal perfusion, leading to renal ischemia, which in turn activates the rennin–angiotensin axis. The production of angiotensin II leads to sodium retention, vasoconstriction and increased sympathetic activity. It also has detrimental effects on nitric oxide production and endothelial function. Renovascular hypertension is the result of this process [22,23].

TMA were present in 6/32(18.8%) patients with 2ry APS and had a highly significant association with renal infarctions that had been detected by DMSA scan as micro thrombi could mechanically obstruct glomerular capillaries, diminishing the blood supply to glomeruli and renal tubules, thereby causing chronic hypoxic/ischemic injuries to the affected glomeruli and tubules. This would in turn decrease the glomerular filtration rate leading to the loss of nephrons and impaired renal function. Clinical studies had indicated that lupus nephritis (LN) patients with glomerular micro thrombi (GMT) had more severe renal tissue injury, poorer response to general treatment and worse renal outcome than patients without GMT [5]. Consistent with these findings, we had demonstrated in the present study that LN patients with GMT had higher damage index (SLICC) than those without. The level of serum creatinine, and proteinuria, as well as the frequency of systemic hypertension, were all significantly greater in patients with GMT. Taken together, GMT may be an important cause of renal injury and renal dysfunction in a subset of patients with LN and this coincides with the results of Hui Zheng and his colleagues [24] and also with those of Imad Uthman and Munther Khamashta who documented that. The development of aPL nephropathy in the context of SLE nephritis increases the risk of a poor renal outcome [25].

Antiphospholipid syndrome nephropathy had been described as a distinct entity found in one third of lupus nephritis patients but independent of the lupus lesions [26]. In the present study APS nephropathy had been detected in (21.9%) of our patients which was a little bit lower than the described percentage and this can be explained by the lower number of SLE patients with 2ry APS taken in the present study, which should be increased in future studies.

APS nephropathy was strongly associated with both aCL and LA, suggesting that APL plays a direct role in the development of APS nephropathy [27] and this also coincides with the results of the present study.

Low density lipoproteins were significantly lower in cases with SLE and 2ry APS, this can be explained by being consumed. This was previously explained by Hasunuma Y. and his colleagues who documented at a molecular level, that anticardiolipin antibodies (aCL) had been shown to have atherogenic properties. For example, aCL can cross react with oxidized low density lipoproteins (ox-LDL), and may enhance the in vitro uptake of ox-LDL by monocytes [28].

Sangle and his colleagues had demonstrated the presence of RAS in (26%) of (77) patients with aPL and uncontrolled blood pressure (60 with SLE and APS, 11 with primary APS, 6 with aPL only). They observed two possible patterns regarding stenotic artery lesions. The most represented pattern was smooth, well-defined and noncritical stenosis distal to the renal artery ostium, these findings are different from atherosclerotic and fibromuscular dysplasia-related lesions. Indeed, the other described pattern seems to be similar to atherosclerotic lesions and had been found in the proximal region to the ostium of the renal artery, sometimes involving the aorta [29]. This coincides with the results in the present study as we found RAS in (21.9%) of patients and they appeared as smooth, well-defined and noncritical stenosis distal to the renal artery ostium, but we did not find proximal lesions.

5. Conclusion

Previously, it was said that, in SLE patients with aPL it is crucial to distinguish between renal failure due to SLE nephritis (immune-complex disease) from that due to APS (glomerular thrombosis). This distinction, which can only be accomplished by kidney biopsy, is critical as the treatment for each syndrome is different. Aggressive SLE nephritis requires cytotoxic therapy, whereas APS nephropathy benefits from anticoagulation. But now we can add that renal MR angiography and renal DMSA can differentiate between the two conditions, which are less aggressive and safer maneuvers than renal biopsy especially in patients with thrombocytopenia accompanying APS.

References

[1] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, Derksen RHWM, DE Groot PG, Koike T, Meroni PL, Reber G, Shoenfeld Y, Tincani Vlachoyiannopoulos PG, Krilis SA. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295–306. doi:10.1111/j.1538-7836.2006.01753.

[2] Conley CL, Hartman RC. A hemorrhagic disorder caused by circulating anticoagulant in patients with disseminated lupus erythematosus. J Clin Invest 1952;31:621–22.

[3] Bowie EJ, Thompson JH, Pascuzzi CA. Thrombosis in systemic lupus erythematosus: despite a circulating anticoagulant. J Lab Clin Med 1963;62:416–30.

[4] Kant KS, Pollack VE, Weis MA. Glomerular thrombosis in systemic lupus erythematosus: prevalence and significance. Med (Baltimore) 1981;60:71–86.

[5] Daugas E, Nochy D, Huong du LT, Duhaut P, Beaufils H, Caudwell V. Antiphospholipid syndrome nephropathy in systemic lupus erythematosus. J Am Soc Nephrol 2002;13:42–52.

[6] Antonietta Gigante, Maria Ludovica Gasperini, Rosario Cianci, Biagio Barbano, Konstantinos Giannakakis, Domenico Di Donato, Giorgio Fuiano, Antonio Amoroso. Antiphospholipid antibodies and renal involvement. Am J Nephrol 2009;30:405–12.

[7] Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus [letter]. Arthritis Rheum 1997;40:1725.

[8] Wilson WA, Gharavi AE, Koike T, Lockshin MD, Branch DW, Piette JC. International consensus statement on preliminary classification criteria for definite antiphospholipid syndrome:

report of an international workshop. Arthritis Rheum 1999;42:1309–11.
[9] Bombardier C, Gladman D, Urowitz M, Caron D, Chang C. Derivation of the SLEDAI A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. Arthritis Rheum 1992;35:630–40.
[10] Gladman D, Ginzler E, Goldsmith C, Fortin P, Liang M, Urowitz M. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum 1996;39:363–9.
[11] Churg J, Sobin LH. Renal disease. In: Churg J, Sobin LH, editors. Classification and atlas of glomerular disease. Tokyo-New York: Igaku-Shoin; 1982. p. 127–49.
[12] Austin III HA, Muenz LR, Joyce KM, Antonovych TA, Kullick ME, Klippel JH. Prognostic factors in lupus nephritis: contribution of renal histologic data. Am J Med 1983;75:382–91.
[13] Manoussakis MN, Gharavi AE, Drosos AA, Kitridou RC, Moutsopoulos HM. Anticardiolipin antibodies in unselected autoimmune rheumatic disease patients. Clin Immunol Immunopathol 1987;44:297–307.
[14] Brandt JT, Triplett DA, Alving B, Scharrer I. On behalf of the Subcommittee on Lupus Anticoagulant/Antiphospholipid antibody of the Scientific and Standardisation Committee of the ISTH. Criteria for the diagnosis of lupus anticoagulant: an update. Thromb Haemost 1995;74:1185–90.
[15] Platt Joel F, Rubin Nathan M, Ellis Ames H. Diabetic nephropathy: evaluation with renal duplex doppler US. Radiology 1994;190:343–6.
[16] Reto Sutter, Daniel Nanz, Lutz Amelie M, Thomas Pfammatter, Burkhardt Seifert, Anja Struwe, Christina Heilmaier, Dominik Weishaupt, Borut Marincek, Willmann Jürgen K. Assessment of Aortoiliac and Renal Arteries: MR Angiography with Parallel Acquisition versus conventional MR Angiography and Digital subtraction Angiography 1. Radiology 2007;245:276–84.
[17] De Sadeleer C, Tondeur M, Melis K. A multicenter trial on interobserver reproducibility in reporting on 99mTc-DMSA planar scintigraphy: a Belgian survey. J Nucl Med 2000;41:23–6.
[18] Hitzel A, Liard A, Vera P, Manrique A, Menard JF, Dacher JN. Color and power Doppler sonography versus DMSA scintigraphy in acute pyelonephritis and in prediction of renal scarring. J Nucl Med 2002;43:27–32.
[19] Patel K, Charron M, Hoberman A, Brown ML, Rogers KD. Intra- and interobserver variability in interpretation of DMSA scans using a set of standardized criteria. Pediatr Radiol 1993;23:506–9.
[20] Dawson B, Trapp RG. Basic and clinical biostatistics. 3rd ed. Mcgraw-Hill Inc; 2001.
[21] Nzerue CM, Hewan-Lowe K, Pierangeli S, Harris EN. ''Black swan in the kidney''. Renal involvement in the antiphospholipid antibody syndrome. Kidney Int 2002;62:733.
[22] Perazella MA, Setaro JF. Renin–angiotensin–aldosterone system:fundamental aspects and clinical implications in renal and cardiovascular disorders. J Nucl Cardiol 2003;10:184–96.
[23] Higashi Y, Sasaki S, Nakagawa K, Matsuura H, Oshima T, Chamaya K. Endothelial function and oxidative stress in renovascular hypertension. N Engl J Med 2002;346:1954–62.
[24] Hui Zheng, Yi Chen, Wen Ao, Yan Shen, Xiao-wei Chen, Min Dai, Xiao-dong Wang, Yu-cheng Yan, Cheng-de Yang. Antiphospholipid antibody profiles in lupus nephritis with glomerular microthrombosis: a prospective study of 124 cases. Arthritis Res Ther 2009;11(3):R93.
[25] Imad Uthman, Munther Khamashta. Antiphospholipid Syndrome and the Kidneys. Semin Arthritis Rheum 2006;35:360–7.
[26] Jha R, Sinha S, Kumar J, Bansal D, Gupta PC. Department of Renal Sciences & Department of Vascular & Endovascular Surgery* Medwin Hospital & Heart Institute, Hyderabad: Renal infarction in antiphospholipid syndrome. Indian J Nephrol 2005;15:17–21.
[27] Tektonidou MG, Sotsiou F, Nakopoulou L, Vlachoyiannopoulos PG, Moutsopoulos HM. Antiphospholipid syndrome nephropathy in patients with systemic lupus erythematosus and antiphospholipid antibodies. prevalence, clinical associations, and long-term outcome. Arthritis Rheum 2004;50:2569–79.
[28] Hasunuma Y, Matsura E, Makita Z, Katahira T, Nishi S, Koike T. Involvement of b2 glycoprotein I and anticardiolipin antibodies inoxidatively modified low density lipoprotein uptake by macrophages. Clin Exp Immunol 1997;107:569–74.
[29] Sangle SR, D'Cruz DP, Jan W, Karim MY, Khamashta MA, Abbs IC, Hughes GRV. Renal artery stenosis in the antiphospholipid (Hughes) syndrome and hypertension. Ann Rheum Dis 2003;62:999–1002.