Case Report

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BILATERAL RENAL ARTERY STENOSIS IN A HYPERTENSIVE LUPUS PATIENT WITHOUT RENAL DYSFUNCTION: A CASE REPORT

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SUMMARY

Systemic lupus erythematosus (SLE) is associated with a high prevalence of atherosclerosis and an enhanced cardiovascular mortality. In adult subjects, several studies have shown the coexistence of SLE and renal artery stenosis, most of them with unilateral involvement or with renal dysfunction.

We observed a 62-year-old man with SLE and a 10-year history of moderate-to-severe hypertension who was admitted to our hospital because of uncontrolled blood pressure values (152/95 mmHg), despite drug therapy. No signs of renal impairment were evident.

After an initial physical examination, which presented a periumbilical bruit, a renal ultrasound was performed with evidence of bilateral renal artery stenosis. An angio-MR study also confirmed the diagnosis and showed a double renal artery on the right side.

Many different factors can contribute to the bilateral renal artery stenosis in this patient. Chronic inflammatory state associated to SLE, metabolic alterations with dyslipidemia and steroid therapy may all be involved in the development of the renal atherosclerotic lesions.

Introduction

Systemic lupus erythematosus (SLE) is associated with a higher prevalence and a more rapid progression of atherosclerosis than the general population (1,2). Studies have shown that lupus patients present a 5-to-6 fold increased risk of coronary and cerebrovascular diseases, and an enhanced cardiovascular mortality (1-4). Moreover, approximately 30% of lupus patients have subclinical atherosclerosis, as the patient age increases at diagnosis, longer is the duration of the disease (2,3).

Atherosclerotic process is the most common cause of renal artery stenosis in the adulthood. Although atherosclerosis is a well-known complication of SLE, only small amounts of data exist about the coexistence of SLE and renal artery stenosis. Most cases show unilateral involvement, impaired kidney function, renal infarction or association with antiphospholipid antibodies (5,6).

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We observed a lupus patient with high blood pressure values and bilateral stenosis of renal arteries without deterioration of renal function and with no evidence of antiphospholipid-antibodies or lupus anticoagulant (LAC).

Case history

A 62-year-old man with SLE, diagnosed by skin biopsy about 20 years ago, and a 10-years history of moderate-to-severe hypertension, treated with amlodipine 5 mg/day, was admitted to our Hypertension Unit because of high blood pressure values. A history of steroid-induced diabetes complicated by mixed peripheral neuropathy, osteoporosis and dyslipidemia was also present. No signs of renal function impairment were evident.

Body mass index, blood pressure (BP) and heart rate were respectively 23.6 Kg/m^2, 152/95 mmHg and 64 bpm. Physical examination did not detect anything abnormal, except for a holosystolic bruit in right periumbilical area.

Laboratory tests showed: hemoglobin 11.8 g/dl, BUN 34 mg/dl, creatinine 0.7 mg/dl, eGFR (EPI) 119 ml/min/1.73m^2, serum sodium 136 mEq/L, serum potassium 4.0 mEq/L, serum total calcium 8.3 mg/dl, total cholesterol 178 mg/dl, c-HDL 35 mg/dl, c-LDL 113 mg/dl, triglycerides 152 mg/dl, serum glucose 150 mg/dl, HbA1c 6%, serum uric acid 6.1 mg/dl, ESR 16 mm/h, CRP 1.8 mg/L, and negative antinuclear, anti-double-stranded deoxyribonucleic acid (dsDNA), antiphospholipid and anti-β2 glycoprotein antibodies, as well as LAC. Normal values were observed regarding standard urinalysis, 24-h albumin excretion rate, plasma renin activity (0.5 ng/ml/h) and plasma aldosterone levels (96 pg/ml), both assessed in a recumbent position and after a two-weeks antihypertensive pharmacological washout.

A 24-h ambulatory blood pressure monitoring during treatment with calcium channel blockers showed the following average BP values: daytime BP 147/87 mmHg and nighttime BP 122/70 mmHg. Therefore, the circadian BP variability was normal (dipper pattern). The aortic pulse wave velocity (12.68 m/s) and aortic augmentation index (42.74%) were also measured by using the Arteriograph device (Tensiomed Kft., Budapest, Hungary). A Doppler ultrasonographic evaluation of the carotid arteries revealed the presence of bilateral calcified non-stenotic plaques on both sides, and the carotid intima-media thickness (IMT) was 1.0 mm.

A renal ecography with Doppler integration was also performed. It showed a normal kidney size and structure, with reduced blood flow velocities but normal values of resistive (RI) and pulsatility (PI) indexes. The examination of the renal artery ostia also revealed reduced vessel diameters

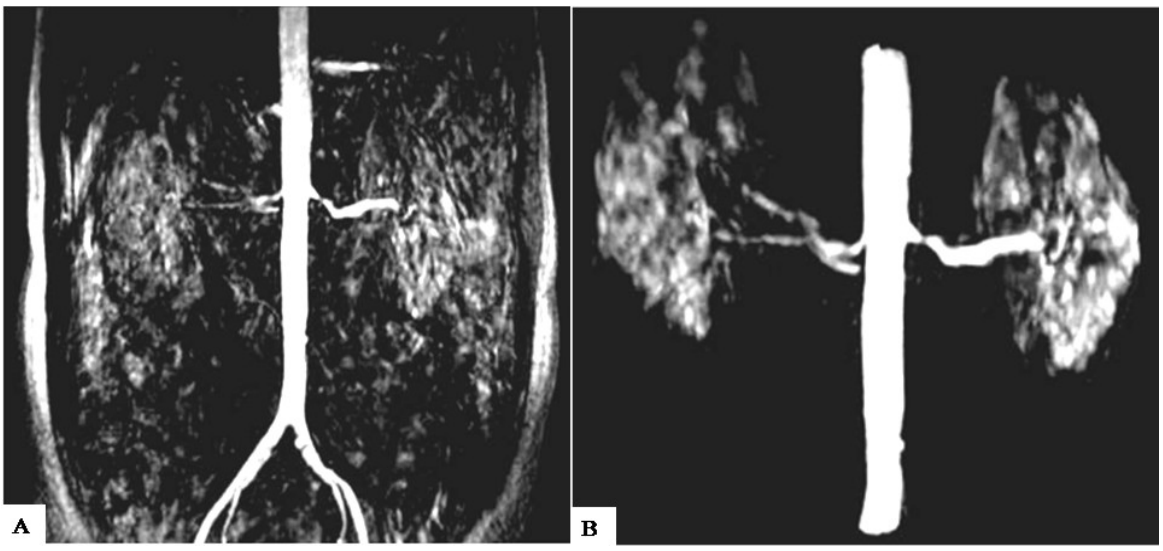

Figure 1: Upper abdomen angio-MR (A) and renal arteries in detail (B). Left renal artery shows a 65% stenosis at about 8 mm from its origin, extending for 5-6 mm. On the right side, a double renal artery is present, with a 90% stenosis of most of the caudal artery

bilaterally (right: 0.39 cm; left: 0.43 cm), with no significant differences between the two sides; in addition, elevated peak systolic velocities (PSV=317 cm/s to the right; PSV=218 cm/s to the left) and increased reno-aortic ratio values (RAR=3.6 on the right; RAR=2.5 on the left) were found. Therefore, the patient underwent a renal vessels angio-MR, that confirmed the presence of bilateral renal artery stenosis (right:90 %; left:65%) and showed the presence of a double right renal artery (Figure 1).

The patient refused to undergo any further invasive procedures. Therefore, a more appropriate pharmacological therapy (amlodipine 10 mg/day, losartan 50 mg/day and chlorthalidone 25 mg twice a week) has been initiated and a 1-year follow-up has been carried out, with satisfactory results regarding BP values and renal function.

Discussion

Atherosclerotic disease is currently recognized as the most common cause of renal artery stenosis in adults. Numerous studies show that atherosclerotic damage has a higher incidence, extension and progression in patients with chronic autoimmune disease compared to the general population (1-4). Even if there is substantial data regarding the presence of unilateral renal artery stenosis in lupus patients, very few cases are reported about the coexistence of bilateral renal arterial stenosis and SLE. Moreover, in all these cases, an impaired renal function or renal infarction have been described (5,6).

The presence of bilateral renal arterial stenosis in a hypertensive patient with SLE without renal impairment has no precedent in the literature. If this association is casual or causal has not been established. However, there is evidence that support the latter hypothesis.

First, some studies emphasize the importance of the chronic inflammation on the genesis of the lesions (2,3,7). Several inflammatory mediators, in particular cytokines overexpressed in lupus patients such as IFN-1, TNF-alfa and low levels of TGF-beta act by altering the processes of endothelial repair, by promoting the migration and the proliferation of vascular smooth muscle cells and by recruiting inflammatory cells. This leads to induction, acceleration and progression of the atherosclerotic lesions, thus contributing to the increased cardiovascular risk in patients with SLE (7,8).

Dyslipidemia is also an important factor involved in atherosclerosis in SLE (3,9). Substantial data, in fact, show that lupus patients, with or without renal dysfunction, have a greater metabolic derangement than the general population (9). Chronic inflammatory states, as well as prolonged steroid therapy, contribute to altering the lipid metabolism. The resulting dyslipidemia facilitates the formation of plaques, according to the classical model of atherosclerosis.

Moreover, the same steroid therapy, as well as a non-aggressive immunosuppressive therapy, may further contribute to the development of vascular wall damage, although conflicting data exists in the literature. In fact, sustained steroid therapy could determine medial necrosis, because of connective tissue disintegration, thus creating a *minoris resistentiae* area more susceptible to local hemodynamic injury (10).

In conclusion, the presence of bilateral renal artery stenosis in our patient seems to have pathogenetic and pathophysiological connections with SLE. Although these assumptions seem to be in agreement with the literature, further studies are necessary to confirm the mechanisms we proposed to explain this unusual vascular finding.

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