

Lastly, we must stress the importance of detecting this disease early, given that the effectiveness of treatment depends on how quickly it is diagnosed. A delayed diagnosis leads to CRF and massive oxalate deposits in organs and tissues. This must be considered for the population at risk: i.e. people from the Canary Islands and Maghrebians. The Canarian population with PHO are not Maghreb but Caucasian, but given that it is an island, a cross over has occurred.

1. Levy M, Feingold J. Estimating prevalence in single gene kidney diseases progressing to renal failure. *Kidney Int* 2000;58:925.
2. Santana A, Torres A, Salido E. Patología molecular de la hiperoxaluria primaria. *Nefrología* 2003;23(Supl 1):90.
3. Hoppe B, Langman CB. A United States Surrey on diagnosis, treatment, and outcome of primary hyperoxaluria. *Pediatr Nephrol* 2003;18:986.
4. Danpure CJ. Metabolic and clinical heterogeneity of primary hyperoxaluria type I. *Am J Kidney Dis* 1991;17:366.
5. Danpure CJ. Advances in the enzymology and molecular genetics of primary hyperoxaluria type 1. Prospects for gene therapy. *Nephrol Dial Trasplant* 1995;10(Suppl 8):24.
6. Hoppe B, Leumann E. Diagnostic and therapeutic strategies in hyperoxaluria: a plea for early intervention. *Nephrol Dial Trasplant* 2004;19:39.
7. Hoppe B, Kemper MJ, et al. et al. Plasmacalcium-oxalate saturation in children with renal insufficiency and in children with primary hyperoxaluria. *Kidney Intern* 1998;54:921.
8. Lorenzo V, Torres A, Hernandez D, et al. Evolución de la enfermedad ósea en pacientes con hiperoxaluria primaria en hemodiálisis. *Nefrología* 1990;10(1):53.
9. Lorenzo V, Álvarez, A, Torres A, et al. Presentation and role of transplantation in adult patients with type 1 primary hyperoxaluria and the I244T AGXT mutation: Single-center experience. *Kidney Int* 2006;1115-9.
10. Lorenzo V, Hernández D, Domínguez M, et al. Oxalosis as a cause of absolute resistance to EPO in chronic hemodialysis patients. *Nephrol Dial Trasplant* 1992;7:1163-4.

M. Martín¹, G. Martín Reyes¹, A. Torres de Rueda¹, R. Toledo Rojas¹, C. Jironda¹, I. García², T. García de la Oliva³, M.L. Pérez Vaca⁴, D. Hernández¹

¹ Nephrology Department. Carlos Haya Hospital. Málaga, Spain.

² Anatomical Pathology Department. Carlos Haya Hospital. Málaga, Spain.

³ Radiology Department. Carlos Haya Hospital. Málaga, Spain.

⁴ Haematology Department. Carlos Haya Hospital. Málaga, Spain.

Correspondence: G. Martín Reyes

Servicio de Nefrología.

Hospital Regional Universitario Carlos Haya.

Almirante Enríquez 10, Bajo D. 29017 Málaga.

Spain.

gmartinr@senefro.org

Diagnosis of secondary hypertension causing miscarriage during the first trimester of pregnancy

Nefrología 2011;31(2):229-31

doi:10.3265/Nefrologia.pre2010.Dec.10677

To the Editor,

Uncontrolled arterial hypertension (AHT) during pregnancy compromises correct gestation development. We describe the case of a 41-year-old pregnant woman who was referred to our unit after having suffered a miscarriage in the tenth week of gestation.

The patient had no personal or family history of interest, and ATH was detected in the eighth week of pregnancy. She visited the emergency department on several occasions due to metrorrhagia and asthenia, with blood pressure (BP) at around 160-170/100-110mm Hg. Alpha-methyldopa was prescribed at 500mg every 8 hours, gradually increasing doses but without adequately controlling AHT. In the tenth week of pregnancy, the patient had a miscarriage and was referred to

the outpatient nephrology unit.

In the physical examination BP was 162/100mm Hg and heart rate (HR) 74 systoles. She had no distal oedemas or other data of interest.

Supplementary tests

1. Haemogram: normal.
2. Biochemistry: creatinine: 0.92mg/dl; glomerular filtration rate (GFR) calculated using MDRD-4 equation: 67ml/min; sodium: 140mEq/l; potassium: 3.3mEq/l; calcium: 9.7mg/dl; uric acid: 4.7mg/dl; GOT: 26IU/dl; GPT: 21IU/dl; LDH: 337IU/l; total bilirubin: 0.3mg/dl; normal coagulation, negative indirect Coombs test.
3. Venous gasometry: normal.
4. Urine: negative systematic and sedimentary tests, microalbuminuria/creatinine index: 8µg/mg; uricosuria: 0.3g/24h.
5. Chest X-ray: no pathological findings.
6. Electrocardiogram: sinus rhythm, no blockages or signs of ischaemia.
7. Funduscopy: normal.
8. Anatomopathological exam of the placenta: normal.

The abdominal ultrasound and renal Doppler scan were normal. Drug treatment was started with calcium antagonists and doxazosin, achieving better pressure control, although it was insufficient. A second analysis found plasma aldosterone of 1161pg/ml and urinary aldosterone of 22.68µg/24h, with a plasma renin activity at baseline of 0.6ng/ml/h and aldosterone/renin rate of 193.3. The remaining parameters (catecholamines in urine, thyroid hormones and plasma cortisol) were all normal. Given the suspected primary hyperaldosteronism (PHA), a saline overload test was performed and 2 litres of physiological saline solution administered over 4 hours. Previous treatment did not have to be modified, however, we do recommend suspending angiotensin-converting enzymes (ACE), angiotensin II receptor antagonists (ARA-II), beta-blockers

and diuretics beforehand.¹ Following the saline overload, aldosterone was not suppressed, being 27.6ng/dl (normal: <10ng/dl). PHA was confirmed as the cause of her secondary AHT and treatment with spironolactone was started, achieving better blood pressure control and relieving her asthenia. The examination was completed with a CT with contrast medium and magnetic resonance imaging, which revealed a 1cm-adenoma in the left suprarenal gland (Figure 1).

At present, BP is controlled with 50mg of spironolactone per day, and the patient is waiting for a left suprarenalectomy to avoid complications in future pregnancies.

This case illustrates the serious complications that are secondary to poorly controlled ATH during pregnancy, such as miscarriage, *abruptio placentae*, and delayed foetal growth, which is likely to be related to vasoconstriction and placental endothelial dysfunction.² The differential diagnosis of ATH during pregnancy involves testing for essential hypertension, pregnancy-related ATH, pre-eclampsia or secondary aetiology.³

Essential ATH. It is difficult to diagnose it during pregnancy if the

patient has not been diagnosed with ATH previously or has not had any BP readings. Pregnant patients diagnosed with chronic ATH present with BP equal or above 140/90mm Hg on two occasions before the twentieth week of the pregnancy, which continues to persist 6 weeks postpartum. Our patient claimed that she had no history of ATH and no lesions to the target organ were found due to ATH.

Pregnancy-related ATH. It is the main cause of hypertension during pregnancy,⁴ and appears during the second half of the pregnancy in patients that were previously normotensive. It is not usually associated with oedemas or proteinuria and BP normalises after the birth, although high BP levels can persist up to 10 days following delivery.

Pre-eclampsia. It is a pregnancy-related disorder, which develops from the 20th week. The patient has arterial hypertension and proteinuria above 0.3g/24h.⁵ Proteinuria may become apparent in advanced phases of the pregnancy, meaning that in principle, pre-eclampsia should not be ruled out when there is no sign of proteinuria, especially if ATH is diagnosed after 20 weeks of pregnancy, with headaches, oedemas or altered laboratory findings (thrombocytopenia, altered hepatic enzymes, hyperuricaemia). New low calciuria levels has been reported to be an early pre-eclampsia marker.⁶ The patient in this case, had ATH before 20 weeks, no analytical alterations were found which would suggest pre-eclampsia.

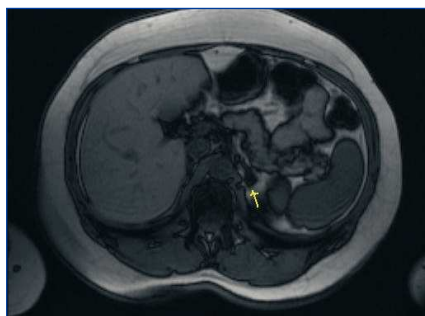
Secondary ATH. Some authors recommend assessing metanephrine and normetanephrine levels and performing an ultrasound scan of the suprarenal gland for patients with recently diagnosed ATH.⁵ This is because a pheochromocytoma could be completely asymptomatic and fatal if not diagnosed before the birth. In

our study, having dismissed previous essential ATH and pre-eclampsia, we investigated the possibility of secondary ATH, and finally diagnosed primary hyperaldosteronism from the supplementary tests mentioned above.

The treatment of choice for ATH secondary to PHA is eplerenone or spironolactone but both of them should not be used during pregnancy due to the potential feminising effect that aldosterone has on male fetuses.⁷ We have found very little evidence of eplerenone use during pregnancy.⁸ Alpha-methyldopa, labetalol and amlodipine can be used as alternative treatments. Surgery should only be indicated during pregnancy for cases that are refractory to conventional treatment⁹ or if patients have adenomas more than 4cm in diameter.⁹ New laparoscopic surgical techniques during pregnancy have lead to greater effectiveness and less surgical risk for the mother and the baby. The retroperitoneal approach has more advantages than the transperitoneal one, given that organ movement is more restricted during the surgical procedure and because it uses much lower intraabdominal pressure.^{10,11}

To conclude, PHA diagnosis is very rare during pregnancy, but it must be taken into consideration because early treatment could reduce severe complications related to poor blood pressure control.

1. Young WF Jr, Kaplan N, Rose B. Approach to the patient with hypertension and hypokalemia. UpToDate 2010. Available at: <http://www.uptodate.com>.
2. Saito Y, Omoto T, Fukuda M. Lobular pattern of choriocapillaris in pre-eclampsia with aldosteronism. *Ophthalmol* 1990;74(11):702-3.
3. Matsumoto J, Miyake H, Isozaki T, Koshino T, Araki T. Primary aldosteronism in pregnancy. *J Nippon Med Sch* 2000;67(4):275-9.
4. Marín R, et al. Hipertensión arterial en el embarazo: estudio 864 casos consecutivos



A left, enlarged adrenal gland and a 1cm-lesion indicative of adenoma (arrow).

Figure 1. MR of left adrenal gland

- observados durante un período de 24 años. *Revista Nefrología* 1999;19(4):308-17.
5. Mancía G, Grassi G, Kjldsen S. Manual de hipertensión de la European Society of Hipertensión. J & C Ediciones Médicas, S.L., 2009;281-7.
 6. Conde-Agudelo A, Belizán JM, Lede R, Bergel E. Prediction of hypertensive disorders of pregnancy by calcium/creatinine ratio and other laboratory tests. *Int J Gynaecol Obstet* 1994;47:285-6.
 7. Okawa T, Asano K, Hashimoto T, Fujimori K, Yanagida K, Sato A. Diagnosis and management of primary aldosteronism in pregnancy: case report and review of the literature. *Am J Perinatol* 2002;19(1):31-6.
 8. Villa Alcázar L. Indicación de la eplerenona en la gestación: no hay experiencia, evitar o sopesar riesgo/beneficio de su uso. *Medimecum* 2008.
 9. Young WF Jr, Kaplan NM. The adrenal incidentaloma: treatment, unilateral adrenal masses. UpToDate 2010. Available at: <http://www.uptodate.com>.
 10. Kosaka K, Onoda N, Ishikawa T, Iwanaga N, Yamamasu S, Tahara H, et al. Laparoscopic adrenalectomy on a patient with primary aldosteronism during pregnancy. *Endocr J* 2006;53(4):461-6. Epub 2006 Jul 5.
 11. Zafer Nursal T, Caliskan K, Ertorer E, Parlakgumus A, Moray G. Laparoscopic treatment of primary hyperaldosteronism in a pregnant patient. *Can J Surg* 2009;52(5):E188-E190. PMID: PMC2769106.

O. Fikri Benbrahim¹, R. García Agudo¹, F. Cazalla Cadenas¹, A. Martínez Calero¹, J. González-Spínola²

¹Nephrology Department. La Mancha-Centro Hospital Complex. Alcázar de San Juan, Ciudad Real, ²Radiology Department. La Mancha-Centro Hospital Complex. Alcázar de San Juan, Ciudad Real, Spain

Correspondencia: O. Fikri Benbrahim
Sección de Nefrología.
Hospital La Mancha Centro.
Avenida de La Constitución, 3.
13600 Alcázar de San Juan. Ciudad Real.
fikrioussamah@yahoo.fr

Cyclophosphamide-induced lupus flare in diffuse proliferative lupus nephropathy

Nefrología 2011;31(2):231-3

doi:10.3265/Nefrologia.pre2010.Nov.10674

To the Editor,

Lupus nephropathy (LN) has a direct impact on the survival of patients with systemic lupus erythematosus (SLE).¹ Twenty percent of LN patients develop an end-stage chronic kidney disease 5-10 years after being diagnosed.² Two phases have been established for treating LN: induction therapy and maintenance therapy.³ We present the case of a patient diagnosed with SLE, who had severe kidney damage. While the patient was undergoing LN induction treatment with steroids and cyclophosphamide, his kidney condition worsened, having developed a severe nephritic syndrome.

The patient was a 22-year-old man, smoker, with personal history of migraines and ventricular extrasystoles. He had been examined by the rheumatology and haematology departments due to thrombocytopenia. He was not allergic to any medication.

The patient attended the emergency department with a fever of >38°C over a 10-day period, with asthenia and joint pain.

On physical examination, he was in a generally good condition, conscious and aware of his surroundings. Blood pressure was 120/80mm Hg; temperature: 38°C; heart rate: 90 beats/min.

He had a bilateral malar erythema and mucocutaneous paleness. He had piercings and tattoos. He did not have jugular ingurgitation, and the rest of the examination was normal.

Biochemical analysis (blood): creatinine: 1.3mg/dl; uric acid:

7.2mg/dl; albumin: 1.7g/dl; total protein: 4.2g/dl; and the remaining parameters were normal. The haemogram showed: haematocrit: 31.3%, thrombocytopenia: 52 000, and an erythrocyte sedimentation rate (ESR) of 22mm/first hour.

In the systematic haematuria sample and white blood count, the 24-hour urine protein was 5.90g/24h and creatinine clearance was 71ml/min.

Immunological test had hypocomplementaemia C3: 45mg/dl (normal value [NV]: 79-152mg/dl); C4: 6mg/dl (NV:16-38mg/dl); normal immunoglobulins; and C-reactive protein: 1.23mg/dl (NV: 0-0.8mg/dl). The autoimmunity test: ANA +1/160 (speckled pattern); anti-DNA: >400; rest of antibodies, negative. Indirect Coombs test was negative. In the blood electrophoretic profile, hypoproteinaemia and hypoalbuminaemia were detected. The coagulation test was normal, with positive IgG and IgM anticardiolipins.

There were no relevant findings from the chest X-ray. We saw that the patient's kidneys were 14.5cm and hyperechogenic in the kidney ultrasound.

The SLE diagnosis was made and a kidney biopsy was performed to assess the kidney damage: 40 glomeruli per cross-section were found and one of them was sclerotic. All of the glomeruli had a similar diffuse proliferative appearance, and more than 50% (36 glomeruli) were associated with an extracapillary proliferation (crescents). Fibrinoid necrosis was also observed in some glomeruli, as well as wire loops and haematoxylin bodies, with positive immunofluorescence: IgG (+++), IgM (+++), IgA (+++) and C3 (+++). No fibrosis or atrophy was found in the interstitial space, but mild non-specific lymphocytic infiltration could be seen. The activity index was 18/24 and chronicity 1/12. The definitive diagnosis was lupus nephropathy type IV.