Self-limiting p-ANCA positive vasculitis in patient with pre-eclampsia

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To the Editor,

Preeclampsia is a common complication of pregnancy (3%-10%) which is defined by the development of high blood pressure and proteinuria beginning at week 20 of the pregnancy. It is associated with a number of factors: family history, thrombophilia, diabetes, etc.[1,2]

With this in mind, we present the case of a 33 year old patient with a history of pulmonary thromboembolism, testing negative for blood clotting disorders (including lupus anticoagulant and anti-cardiolipin) but presenting a heterozygous deficiency in methylenetetrahydrofolate reductase enzyme gene (C677T) who developed partial HELLP syndrome during week 34 of gestation. The treatment approach consisted of administering hydralazine and alpha-methyldopa, and in the end, an emergency caesarean section. However, clinical resolution was only partial (with residual proteinuria of 113mg/dl in 24 hour urine sample).

Four months later (during the lactation period), the patient suffered a new episode, characterised by inflammation in both ankles, hypertension and decreased renal function with no oliguria (urea 145mg/dl, creatinine 4.3mg/dl) and was then admitted in the nephrology department. Relevant test results were haemoglobin: 9.5g/dl; albumin: 4.3g/dl; microhaematuria; and proteinuria of 125mg/dl. The immunology study showed that she was positive for antinuclear antibodies (ANA 2.02 at titres of 1:80) with normal anti-DNA antibodies, antihistone antibodies and a complement levels. Anti-cytoplasmic antibodies (ANCA) were positive at low titres (26.4U/l) with anti-myeloperoxidase specificity (ANCA-MPO). However, the patient's condition started to improve spontaneously under conservative treatment, which allowed us to delay the renal biopsy until after the lactation period. The subsequent histopathological study described sclerosis in 40% of the sample, with obliteration of capillary lumens due to mesangial proliferation and endotheliosis, increase in mesangial material and capsular adhesions. Parietal epithelial cells were especially prominent and formed fibrous epithelial crescents in 4 glomeruli (30% of the sample). On the other hand, podocytes were very swollen with numerous protein reabsorption droplets. Predominantly lymphocytic inflammatory deposits and mild focal fibrosis were observed in the interstitium. Immunofluorescence revealed small diffuse deposits of IgG and C3 located in the mesangium with an intensity of 1+ (Figure 1).

Based on these data, we prescribed combination therapy with prednisone 1mg/kg/day and azathioprine 2mg/kg/day. Progress remained favourable; anaemia was corrected and renal function returned to normal levels (urea 41.2mg/dl, creatinine: 1mg/dl), as did autoantibody levels. However, the 24 hour urine test still revealed microhaematuria and proteinuria (203.5mg/dl). In order to screen for a possible pulmonary disorder, which is common in microangiopathies, pulmonary function tests were performed which showed decreased alveolar diffusion due to the capillary action.

Lastly, we re-considered the definitive diagnosis for this case based on the following premises: lack of criteria sufficient to indicate lupus or microscopic polyangiitis; self-limiting renal disease; lack of immunological specificity (concomitant presence of ANA and p-ANCA); histological changes partially compatible with

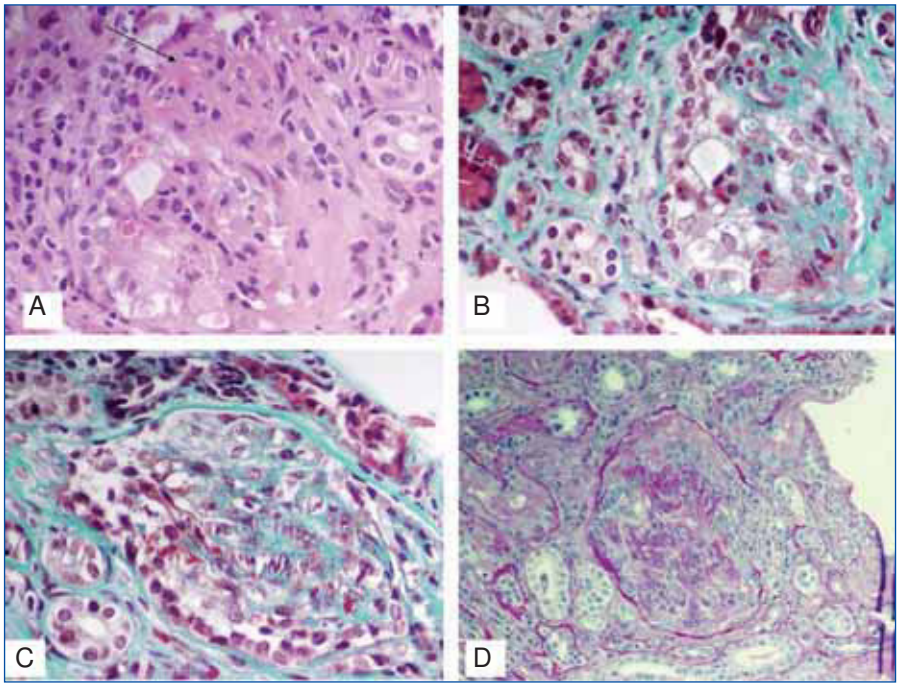

Figure 1. Renal Biopsy. Preeclamptic lesions and fibrous crescents
Increased size of glomeruli and areas of segmental obliteration of capillaries due to endotheliosis (arrow) (A). Areas with segmental sclerosis, swelling of the podocytes showing protein reabsorption droplets inside them (A, B, C) and proliferation of parietal epithelial cells with formation of incipient (A) and fibrous (D) crescents.

preeclamptic damage (such as endotheliosis, mesangial proliferation and even interstitial fibrosis); and most of all, the course of the disease being related to childbirth.[3] The final diagnosis was drug-induced p-ANCA vasculitis in conjunction with toxaemia. In this case, systemic symptoms may have been related to prior intake of hydralazine and/or methyldopa. In addition, its episodic nature fully coincides with the autoimmunity-promoting effect described in the literature for both drugs; in the case of hydralazine, this also seems to be linked to the development of some types of pulmonary-renal syndrome and ANCA-positive pauci immune glomerulonephritis.[4,5]

Conflicts of interest

The authors affirm that they have no conflicts of interest related to the content of this article.

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Medullary aplasia in c-ANCA positive patient with end-stage lupus nephritis

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To the Editor,

Autoimmune processes affecting the kidneys are heterogeneous clinical entities and their differential diagnosis is complex. The best example is systemic lupus erythematosus (SLE), whose pleomorphisms can range from skin or joint lesions to lupus nephritis (LN). Its diagnostic criteria were revised in 1997 by the American College of Rheumatology (ACR), and by following them, the syndrome can be defined with a sensitivity and specificity of 96%.[1] However, atypical clinical profiles are hard to interpret, and the symptoms in such cases are often anachronical and non-specific.

In this context, we present the case of a 40 year old patient with a history of smoking, obesity and high blood pressure (HBP) with no pharmacological treatment. The patient was admitted to the nephrology department because he had experienced fever, diarrhoea/vomiting, weight loss, and progressive decrease in diuresis for 3 weeks. Laboratory results then showed severe renal dysfunction (urea 383mg/dl; creatinine 20.3mg/dl), hypoalbuminaemia (2.3g/dl) and anaemia (haematocrit 20%; haemoglobin 6.9g/dl; mean cell volume 88 fL). Meanwhile, complementary tests found microhaematuria, blood clotting disorders (prothrombin activity 89%; haptoglobin 298mg/dl; reticulocytes 1.5%; low schistocytosis; positive direct Coombs test) in addition to abnormalities found by ultrasound (normal-sized kidneys with cortical hyperechogenicity). In light of these results, and suspecting a glomerular process, with incomplete data suggesting haemolytic anaemia, we performed emergency haemodialysis and a blood transfusion.

Other results gathered at the same time were as follows: negative stool and blood cultures; negative serology for bacteria and parasites; viral serology for hepatitis B, C and HIV showing positive IgM and IgG for cytomegalovirus (CMV), Coxsackievirus, herpes simplex and herpes varicella zoster; and decreased C3 fraction (51mg/dl). A renal biopsy showed generalised glomerulosclerosis in 60% of the sample, with fibrous crescents (some glomeruli showing poorly defined margins), cystic tubular atrophy, fibrosis and interstitial lymphocytic infiltrate. There were also signs of proliferative arteriopathy having to do with HBP (Figure 1).

With a presumed diagnosis of rapidly progressive extracapillary glomerulonephritis (GN) against the diagnosis of SLE, we administered adjuvant immunosuppressive drugs with dialysis (prednisone 1mg/kg/day and azathioprine (AZA) 2mg/kg/day) while waiting for immunology test results. Tests found the following results: ANA (+) at a titre of 1:640; anti-dsDNA (+) 126IU/ml; anti-Sm (+) 1.54U/ml and c-ANCA (proteinase 3-specific cytoplasmic antineutrophil cytoplasmic antibodies) (+) 52.8U/ml. Anticardiolipin and lupus anticoagulant antibodies were negative. This was sufficient to diagnose the syndrome as WHO class VI lupus nephritis in a systemic context (syndrome met 5 of the ACR criteria: nephritis, serositis, abnormal blood tests, ANA at high titres, anti-dsDNA and anti-Sm). Despite the positive results and