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C4d as a diagnostic tool in membranous nephropathy

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To the Editor,

In a recent issue of Nefrología (vol. 32, issue 3, 2012), Espinosa-Hernandez et a. published a study titled *"C4d como herramienta diagnóstica en la nefropatía membranosa"* (C4d as a diagnostic tool in membranous nephropathy).[1] In the introduction, the authors pointed out that the information regarding C4d deposition in glomerular nephropathies is very scarce, and set the objective of their study to determine whether immunohistochemical detection of C4d in patients with membranous nephropathy (MN) could be useful as a diagnostic tool. In the discussion, they pointed out that the information on the role of C4d in MN is limited to a single study of 12 patients using immunofluorescence, published in 1989.[2] They concluded their study by indicating that C4d detection using immunohistochemistry is a very useful tool for the differential diagnosis of MN and minimal change disease.

However, Espinosa-Hernandez et al omitted our publication titled "C4d immunohistochemical staining is a sensitive method to confirm immunoreactant deposition in formalin-fixed paraffin-embedded tissue in membranous glomerulonephritis".[3] In this article, we showed that there was a characteristic glomerular, granular C4d deposit in the basal membrane in 31 cases (100%) with idiopathic MN and in 5 cases (100%) with pure membranous lupus nephritis, class V, following fixation in formalin, paraffin embedding, and immunoperoxidase-based detection. In all cases, the previous diagnosis of lesions was made by immunofluorescence. In addition, in 19 cases with different glomerulonephropathies, including IgA nephropathy, membranoproliferative glomerulonephritis type I, focal segmental glomerulosclerosis, and minimal change disease, we found several reproducible patterns of C4d deposits, without intrinsic background staining. Our results showed that C4d staining in tissues fixed in formalin and embedded in paraffin can be used to detect membranous granular deposits of complement factor in MN. This method proved to be so reliable that it might obviate the need for further biopsies when glomeruli in frozen slides or ultrafine slides for electron microscopy are not available. We concluded our article by indicating that immunostaining using the immunoperoxidase method deserves recognition as a complementary method for the biopsy-based diagnosis of MN.

We would like to see our article receive the recognition it deserves.

Conflicts of interest

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

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Author's reply: C4d as a diagnostic tool in membranous nephropathy

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To the Editor,

Dr. Fernando Val-Bernal and his collaborators commented that we have

omitted in the bibliography a reference to their work published in the November 2011 issue of Histol Histopatho. We believe that "omitting" is not the word that best reflects what happened.

We have been working since 2008 in the study of the C4d in glomerular diseases, and in particular in membranous nephropathy. The results were presented for the first time in the XXXVII Congress of the Andalusian Society of Nephrology, held April 16th-18th 2009, and in the congress of the Spanish Society of Nephrology held in Pamplona that same year. The Public Health System of Andalusia recognized them in 2010 in the Bank of Innovative Practices, whose web site may be accessed.

We wrote our work to initiate the process of publication in the summer of 2011 and sent it to the nephrology magazine [Nefrologia] on November 23, 2011. The article by Dr. Val-Bernal et al., was published in the November issue of 2011. It is obvious the reason why we were not able to detect it in our bibliographic reviews; in addition, we did not know of its existence as we had not seen it on any of our meetings.

We are very glad that Spanish colleagues have reproduced our results, which adds value to both works. We deeply regret not having detected the work of Dr. Val-Bernal et al. in those few days and, as a result, not being able to add it to the bibliography.

The work of Dr. Fernando Val-Bernal is really respectable and the fact that it has not been included in the bibliography does not detract merit from it.

The merit and respect of works is earned by their virtues - and the work of Dr. Val-Bernal has many-, and that of people, by their acts.

Conflicts of interest

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

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B) BRIEF PAPERS ON RESEARCH AND CLINICAL EXPERIMENTS

Gross haematuria in patients with nutcracker syndrome

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To the Editor,

Among the different diagnostic algorithms that are commonly used in outpatient nephrology consultations, nutcracker syndrome/phenomenon is a very rare cause of haematuria. This type of haematuria originating from the left collecting system and is secondary to compression of the left renal vein between the superior mesenteric artery and the aorta.

We herein report the case of a 22-year-old male with no personal or family history of relevance, who was referred to a nephrological department for haematuria. Laboratory analyses confirmed the presence of haematuria that ranged between gross (macroscopic) haematuria and microhaematuria, depending on the measurement. This condition arose both with and without physical exercise. During periods in which urine samples came up clear, microhaematuria was always present. Also, haematuria was not correlated with respiratory tract infections at any level. The patient did not have oedema, abdominal pain, or any other symptoms.

A physical examination revealed the following: weight: 65kg; height: 1.80m; body mass index: 20kg/m^2; blood pressure: 110/60mm Hg; all other measurements were normal. A laboratory analysis revealed the following values: C-reactive protein: 0.9mg/dl; proteinuria: 1g/24 hours; urinary sediment >30 000 red blood cells per field, with no casts or dysmorphic blood cells. The patient also had normal renal ultrasound images. An axial computed tomography angiography (CTA) (Figure 1 and Figure 2) was used to evaluate renal vascularisation, and led us to the diagnosis.

DISCUSSION

Nutcracker syndrome consists of haematuria originating from the left collecting system secondary to compression of the left renal vein, between the superior mesenteric artery and the aorta and is due to a reduced angle between these two arteries. This compression translates into increased pressure on the left renal vein system, which causes varicosities in the renal pelvis and ureter, which can in turn communicate with the urinary tract and cause haematuria. The predisposing factors include: nephroptosis, lumbar hyperlordosis, and reduced peri-renal fat (which was present in our patient). Clinically, this condition can be silent or involve episodes of macroscopic or microscopic haematuria, which can be accompanied by pain in the left renal fossa and/or abdominal pain. The haematuria is usually more intense during orthostasis and exercise, which occurred in our patient. It can also be accompanied by mild proteinuria and can even be asso-