Membranous glomerulonephritis in a patient with syphilis

Nefrologia 2011;31(3):372-3

To the Editor,
La glomerulonefritis membranosa Membranous glomerulonephritis (MGN) is the second most prevalent renal pathology to be identified in biopsies. One of the most common causes of nephrotic syndrome in the adult population, it is characterised by the formation of immune complexes, predominantly IgG and complement, on the subepithelial side of the glomerular capillaries, and this is associated with increased proteinuria.

In general, its aetiology is idiopathic or primary and, less frequently, secondary (immunological, infectious, drug and medication-related, or neoplastic).

Unfortunately, it is difficult to distinguish primary from secondary forms by historical means; so explicit clinical information, including the age of the patient, history of exposure to medicines or toxic substances, serological tests and suspected neoplasias which are linked to the pathology, is required.

The importance of serological tests lies in their ability to confirm the diagnosis. In the case of syphilis screening, non-treponemal tests are performed: the VDRL (Veneral Disease Research Laboratory) and RPR (rapid plasma reagin) tests. If the results are positive, the more specific treponemal tests are performed to confirm the diagnosis: FTA-ABS (absorption of fluorescent antibodies by Treponema) and MHA-TP (Treponema pallidum microhaemagglutination). They must be repeated three and six months later to ensure the response to treatment.

The case which concerns us is relevant, owing to the small number of publications on the association between syphilis and MGN.

The patient was a 27-year-old, white, Caucasian male with a history of cryptorchidism, adenoidectomy and angiod streaks in childhood. He was an active smoker, a social drinker and a homosexual. Two months before being assessed by our department and coinciding with a slight pharyngodynia, an induration had appeared in the patient’s right groin, as well as ulcerated serpiginous lesions on the penis and a whitish urethral discharge, which was initially treated with azithromycin. While waiting for the serological results, maculopapular lesions were observed in the surrounding area on the thighs and trunk. They spread to the patient’s feet and hands, progressing through different phases with no signs of fever, and accompanied by oedema of the lower limbs and genitals, with a slight increase in the abdominal perimeter and a decrease in diuresis, which is why the case was reported to us. The patient’s urine was normal in colour, with no evidence of dysuria or blood in the urine. Blood pressure (BP) was within normal limits.

The analytical findings of note were as follows: urea: 61mg/dl; creatinine: 1.73mg/dl; normal ions; total protein: 4.4g/dl; albumin: 1.8g/dl; total cholesterol: 295mg/dl, HDL: 61mg/dl, LDL: 206mg/dl; triglycerides: 140mg/dl and normal hepatic enzyme levels. Significant findings in the urine analysis included proteinuria: 13.4g at 24h, 250 red blood cells per microlitre and a negative leukocyte count. The haemogram and coagulation were normal, except for an FTP of 762g/l. Autoimmunity assays: anti-nuclear antibodies (ANA) and anti-neutrophil cytoplasmic antibodies (ANCA) negative; complement and protein tests were normal. Serology tests for hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency (HIV) viruses were negative. Positive 1/32 titre RPR (rapid plasma reagin) and FTA (anti-Treponema antibody) results.

Renal ultrasound showed the kidneys to be normal in size. The echocardiogram was within normal limits and no lung parenchyma changes were detected in the chest X-ray.

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Given that the data indicated a nephrotic syndrome, a renal biopsy was performed and 13 glomeruli were counted. They were very slightly enlarged with permeable capillary lumens and no mesangial proliferation or associated inflammatory component. When Masson’s trichrome procedure was used, frequent fuchsinsstained deposits were observed on the subepithelial side of the capillary walls. With methenamine silver no spikes were recognised. There was no increase in fibrous tissue in the interstitium. There were areas of chronic inflammatory infiltration, predominantly containing dispersedly distributed lymphocytes and eosinophils, located around the glomerulus. The tubules contained occasional hyaline cylinders and haematic material. The blood vessels were normal. Immunofluorescence revealed intense granular IgG deposits on the capillary walls and non-specific traces of IgM. Anatomopathological diagnosis: stage 1 MGN.

Treatment was initiated by administering 2.4 million units of intramuscular penicillin G benzathine, intravenous diuretics, and anti-thrombotic and lipid (cholesterol)-lowering prophylactic drugs.

The patient responded favourably and blood volume and renal function returned to normal values (urea 43mg/dl, creatinine 1.28mg/dl) with a clearance rate of 85ml/min/1.73m². At a check-up the following month the proteinuria had disappeared. 1/2 titre RPR values were obtained at three months and they were negative at six months.

Syphilis is a sexually transmitted disease (STD) which is caused by a spirochete called T. Pallidium. It can be transmitted by sexual contact (the most common form of transmission), congenitally via the placenta, or as a result of an infected blood transfusion or accidental inoculation. It is known as ‘the great simulator’, owing to its range of clinical presentations. Primary syphilis manifests as an ulcerated lesion or chancre, which appears two-six weeks after infection. Secondary syphilis is the result of its dissemination via the blood or lymph and its symptoms are highly varied. Tertiary syphilis appears months or years after infection if it has not been properly treated.

In developed countries, largely due to the discovery of penicillin, syphilis was practically wiped out in the 1950s. In the 1980s, owing to the concern about the AIDS epidemic, sexual behaviour changed and an even greater decrease in its incidence was observed. In recent years we have been witnessing a resurgence of this disease in Spain, with an increase in its incidence from 2.57 cases per 100 000 inhabitants in 1995 to 5.70 per 100 000 in 2008, and this is also happening in other European countries and the United States. The new cases occur predominantly in young homosexual men and a large proportion of them present coinfection with HIV (20%-70%, depending on the area in question). Perhaps this is due to a relaxation in sexual behaviour as a result of a reduction in protective measures following the appearance of highly active antiretroviral therapy (HAART) against HIV.

Although the association between syphilis and renal disease has been known for over 100 years, there are few cases reported in Spain in reviews on the subject, which makes diagnosis more difficult, as it is seldom suspected in clinical practice.

Syphilis can cause a wide variety of clinical and pathological forms of renal disease. In addition to MGN, rapidly progressive GN, diffuse endocapillary GN with or without extracapillary formation or minimal change GN have been described. Proteinuria is the most common clinical manifestation. The definitive diagnosis is confirmed by renal biopsy.

It is important to know the age of the patient and to obtain a detailed clinical history when dealing with nephrotic syndrome. Although it is more common for MGN to be associated with HBV than syphilis, we must not forget that, in the battery of serological tests requested in a case of nephrotic syndrome, diagnostic tests for syphilis should be included, more so knowing that there has been a substantial increase in the number of cases in Spain in recent years.

In our case, the patient had been diagnosed with syphilis before and its association with nephropathy facilitated the aetiological diagnosis of MGN. After starting specific treatment (penicillin G benzathine) to eliminate the triggering factor, the nephrotic syndrome remitted.

This experience has made us see that it is of vital importance to conduct a detailed assessment when dealing with a case of nephrotic syndrome. Once we have an exact result and diagnosis, this will enable us to adopt an economic, effective and, above all, curative approach.


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