FOLLOW UP OF 2 PATIENTS WITH MESANGIAL IgA GLOMERULONEPHRITIS EXPOSED TO CADMIUM AND ORGANIC SOLVENTS

AUTHORS: Jaime Fernández*, Pere Sanz**, Santiago Nogué**
* Unit of Toxicology. Laboratorio de análisis Dr.Echevarne. Barcelona ( Spain ) jfernandez@echevarne.com
** Unit of Toxicology. Hospital Clinic. Barcelona ( Spain )

INTRODUCTION: Cadmium and some organic solvents are potentially nephrotoxic. IgA nephropathy, also called Berger’s disease, is a kidney disorder in which antibodies to a protein called IgA accumulates in the kidney.

Two workers diagnosed with IgA mesangial glomerulonephritis who had the antecedent of having been exposed to cadmium and organic solvents have been followed up during several years.

CASE REPORT 1:

47 year old male, non smoker, diagnosed of IgA mesangial glomerulonephritis. Worker for 12 years as a welder in a company making alloys used to cut mable and granite. An autogenous system of welding was employed as support of metal rods consisting of silver (39%), cadmium (26%), copper(21%) and zinc (14%).

The environmental level of cadmium in his workplace was 52 µg/m3 (TLV-TWA: 10 µg/m3). The patient had proteinuria of 2000 mg/l, microhematuria of 150 red blood cells/high power field (rbc/hpf), cadmium in blood of 45 µg/l ( BEI: 5µg/l ) and cadmium in urine of 25 µg/g creatinine ( BEI: 5 µg/g creatinine ). The patient was dismissed from his job and was followed annually for 7 years. In year 7 the cadmium concentrations in blood was 7 µg/l , proteinuria 430 mg/l and creatinine in serum 1,03 mg/dl.

Treatment: Enalapril 10 mg/day.

DIAGNOSIS:
A renal biopsy was carried out that showed five glomeruli, one of which was sclerosed; the rest showed a mild segmentary hypercellularity, and in two a segmentary extracapillary proliferation in the fibrocellular stage was observed, while the interstitium showed foci of fibrosis with tubular atrophy. Immunofluorescence study highlighted that 20% of glomeruli were IgA mesangial nephritis and mesangial pattern. A diagnosis of focal type IgA mesangial glomerulonephritis was made.

FIGURE 1A Renal biopsy

FIGURE 1B Immunofluorescence study

COMMENTS:
The main target organs following exposure to cadmium are the lungs, kidneys, bones and haematopoietic system (Davidson et al, 1988, Thun et al, 1989, Fernandez et al, 1996). While the proximal tubule is a major target in cadmium-induced nephropathy, renal glomeruli are also exposed to circulating metals during plasma filtration, and may also be targets of cadmium toxicity (Xiao et al, 2009).

Several publications show a higher incidence of renal dysfunction in workers with cumulative cadmium concentration in blood below 10 µg/l (Mason et al, 1988; Jarup et al, 1988). Also Bernard et al at 1990 reported the absence of tubular effects and the presence of subtle glomerular dysfunction (increased excretion measured by a very sensitive assay) in workers with a cadmium concentration below 10 µg/l.

A number of publications show an increased excretion of markers of renal dysfunction in workers with cadmium concentrations in urine between 5 and 10 µg/g of creatinine. The most commonly studied markers are the low-molecular-mass proteins (Roels et al, 1981).

The patient exposed to cadmium, even after avoiding exposure had high concentrations of cadmium in blood and urine, and proteinuria, but maintained normal renal blood tests.

CASE REPORT 2:

50 years old male, non smoker. In 2005 a slight proteinuria and microhematuria was detected. For 23 years he worked at a company that makes plant protection products and he was exposed to a large number of substances including organic solvents (acetone, acetonophenone, cyclohexanone, naphtha, toluene and xylene).

Three years ago he was diagnosed of diffuse mesangial proliferative glomerulonephritis with IgA deposits, despite which he continued working until a year ago when he was diagnosed of stage 3 chronic kidney failure secondary to renal disease. The renal blood tests in the past five years showed : serum creatinine 1.4-1.7 mg / dL, microhematuria of 0-58 rbc / hpf, proteinuria 0-2200 mg/24h. After a few months avoiding toxic exposure, proteinuria and hematuria were normalized but serum creatinine remained high.

Treatment: Candesartan exiletil 16 mg/day, Ramipril 5 mg/day and Atorvastatin calcium trihydrate 10 mg/day. Decreasing doses of Prednisone ( initiated at 40 mg/day ; now 15 mg/day).

DIAGNOSIS:
The renal biopsy study highlighted that 20% of glomeruli showing severe sclerosis, 10% were obliterated, there was interstitial fibrosis, tubular atrophy, discrete chronic inflammatory infiltrate. With immunofluorescence diffuse mesangial deposits of IgA and C3 were detected.

COMMENTS:
Exposure to solvents has been associated with acute tubular necrosis, interstitial disease and several histological types of glomerulonephritis and chronic glomerulonephritis (Roy et al, 1991, Porro et al, 1992, Brautbar, 2004).


In another study (published in the Occupational and Environmental Medicine), Jacob et al, 2007 studied 269 patients with different types of glomerulonephritis, including IgA nephropathy. They found that those exposed to solvents, ketones group, had 13 times more risk of initial glomerulonephritis complicated with chronic kidney disease, the exposed to petroleum products had 8.7 times more risk of exposure to toluene or xylene had 8.7 times more risk of chronic kidney disease.

In our case the patient exposed to solvent after avoiding exposure showed microhematuria and proteinuria that were normalized but his renal function remained impaired.

LABORATORY TEST. REFERENCE INTERVAL
Creatinine: 0,66 – 1,09 mg/dl
Proteinuria: Until 150 mg/24 horas
Microhematuria: Absence

CONCLUSIONS: Exposure to chemicals at work may be a potential health risk. Each chemical substance has one or more target organs and its function should be periodically evaluated during the working life and even in cases with overexposure to cadmium, the control must be carried out when the exposure has stopped. It’s important to detect and control occupational exposures to chemicals in those workers particularly sensitive to them. These two workers should be regarded as particularly sensitive to exposure to nephotoxic substances and should avoid this exposure.