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CASE REPORT

Chronic overexposure to cadmium fumes associated with IgA mesangial glomerulonephritis

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Background	Cadmium is a metal used in the zinc, copper and steel industries, and in the manufacture of electric batteries and solar cells. Acute cadmium poisoning is characterized by irritation of the respiratory tract, while in chronic poisoning the main target organ is the renal tubule.
Aims	We report a patient with chronic work overexposure to cadmium, who presented a IgA mesangial glomerulonephritis with no respiratory or renal tubule involvement.
Case report	A 39-year-old patient was referred to our hospital for evaluation of a glomerular nephropathy. For the past 12 years he had worked as a welder, using cadmium electrodes. The patient had no respiratory symptoms and the chest X-ray was normal. Tests showed a proteinuria of 2 g in 24 h with microhaematuria [150 red blood cells/high power field (rbc/hpf)], with preservation of the renal function (creatinine clearance of 137 ml/min). The concentrations of cadmium in blood and urine were 45 μg/l and 25 μg/g creatinine, and an environmental study showed that levels of cadmium in the workplace were 52 $\mu g/m^3$. A renal biopsy showed an IgA mesangial glomerulonephritis. The patient ceased to work with cadmium, and 1 year later cadmium levels had decreased and renal function was found to be stable.
Conclusions	IgA mesangial glomerulonephritis is a disease of unknown aetiology which has been associated with other diseases. Chronic overexposure to cadmium may contribute to the development of this nephrophathy.
Key words	Cadmium exposure; IgA mesangial glomerulonephritis.
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Introduction

Cadmium is a by-product of the zinc and lead industry. It is mainly used in metal plating and in the production of batteries, pigments, plastic stabilizers and some alloys.

After inhalation of cadmium fumes, 10–50% may be absorbed, depending on particle size and chemical composition. Cadmium mainly accumulates in the kidneys and the liver, organs which account for roughly 70% of the total body burden. The half-life of cadmium is about 6 weeks for the fast compartment of cadmium concentration in blood [1]. Excretion is primarily through the kidney, but elimination of accumulated cadmium is very slow with a half-life of 20–40 years.

The main target organs following exposure to cadmium are the lungs, kidneys, bones and the haematopoietic system [2–7].

We describe the case of a welder exposed to high levels of cadmium fumes and who was diagnosed with a focal IgA mesangial glomerulonephritis.

Case report

A 39-year-old man, who had smoked one packet of

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cigarettes a day for 15 years, was referred to our hospital to evaluate the recent appearance of proteinuria and microhaematuria.

The patient had worked for 12 years as a welder in a company making alloys used to cut marble and granite. An autogenous system of welding was employed which used electrodes consisting of silver (39%), cadmium (25%), copper (22%) and zinc (14%), of which ~1 kg per week was used. In the workplace, there was no system to extract gases or fumes and no individual respiratory protective equipment was used.

At his first visit to our hospital, the patient was asymptomatic. Direct questioning revealed no signs or symptoms of hepatic or intestinal dysfunction or systemic illness. The patient's general health was good, the physical examination was normal and the BP was 105/65 mmHg. Chest X-ray and ECG were normal. The blood count, general biochemical tests and hepatic parameters were normal. The patient had a proteinuria of 2 g/24 h and a microhaematuria of 150 red blood cells/high power field (rbc/hpf), together with high levels of cadmium in the blood [45 μg/l; biological exposure index (BEI) = 5 μg/l) and urine (25 μg/g creatinine; BEI = 5 μg/g). The patient ceased to work with cadmium after a study revealed that the environmental level of cadmium in his workplace was 52 $\mu g/m^3$ [TLV – TWA (threshold limit values – time-weighted average) = 10 $\mu g/m^3$].

One month later, the patient had a proteinuria of 1.77 g/24 h of glomerular origin; urine concentrations of beta-2-microglobulin, *N*-acetyl-glucosaminidase and retinol-binding protein were normal, the microhaematuria persisted (50–100 rbc/hpf) and good renal function was maintained (creatinine clearance 137 ml/min). Anti-DNA and anti-tissue antibodies were negative, and the complement was normal. Serum immunoglobulins were within normal limits, except for an IgA level of 4.12 g/l (normal values = 0.66–3.65 g/l). The level of cadmium in the blood was 20 μg/l and that in the urine was 50 μg/g creatinine. An abdominal ultrasound showed that the kidneys were of normal size without dilation of the ureter.

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. Inmunofluorescence was positive for C3 (+++) and IgA (++) with a mesangial pattern. A diagnosis of focal type IgA mesangial glomerulonephritis was made and treatment with enalapril 10 mg/day was begun.

A year later, the patient remains stable. A proteinuria oscillating between 1.9 and 3.2 g/24 h and a microhaematuria (50–100 rbc/hpf) persist. Renal function continues to be good (creatinine clearance of 141 ml/min) with normal concentrations of beta-2-microglobulin, *N*-acetyl-glucosaminidase and retinol-binding protein in the urine. Levels of cadmium have decreased to 9 μg/l in the blood and 8 μg/g creatinine in the urine.

Discussion

There is evidence that the kidney is the main target organ of cadmium toxicity following extended exposure to cadmium [6–8]. The proteinuria caused by cadmium exposure is characterized by the presence in urine of a number of low-molecular-weight proteins, including beta-2-microglobulin, lysozyme, ribonucleases, immunoglobulin light chains and retinol-binding protein. These low-molecular-weight proteins are all readily filtered by the glomeruli and are normally reabsorbed in the proximal tubule of the kidney. Therefore, elevated urinary excretion of these proteins is symptomatic of proximal tubular damage. Urinary excretion of high-molecular-weight proteins such as albumin has also been reported in occupationally exposed workers, but there is some debate as to whether this represents glomerular damage [7] or severe tubular damage [9]. The critical concentration of cadmium in the renal cortex associated with increased incidence of renal dysfunction in an adult human population chronically exposed to cadmium has been estimated to be ~200 μg/g wet weight by several investigators [10]. Cessation of cadmium exposure generally does not lead to any decrease in proteinuria in occupationally exposed workers [9,11].

IgA mesangial glomerulonephritis, described by Berger and Hinglais in 1968 [12], is characterized by diffuse, predominantly IgA deposits in the glomerular mesangium. The disease, typically found in adolescents and young adults, is one of the most frequent causes of recurring macroscopic haematuria and accounts for ~20% of primary glomerular nephropathies. In the Mediterranean region, the incidence of new cases is between 15–40 per million population/year. The aetiology is unknown, but the nephropathy is due to the deposition of circulating immunocomplexes, which mainly contain IgA and sometimes are associated with other diseases such as inflammatory enteropathy, ankylosing spondylitis and psoriasis [13]. However, until now, an association with environmental toxins in general or with cadmium in particular has not been described, although in the case reported here a casual association between the overexposure to cadmium and the glomerular nephropathy cannot be ruled out.

This case illustrates the importance of adequate health and safety conditions in the workplace, and emphasizes that cadmium should, where possible, be progressively replaced in industrial processes, both because of its association with elevated levels of nephrotoxicity and because it is catalogued as a group 1 carcinogenic agent

by the IARC. When cadmium cannot be substituted, workers should be protected by an adequate system of fume and gas extraction, by the use of personal protective equipment and with appropriate health surveillance. In addition, patients with nephropathies should be considered as at high risk and should never be exposed to nephrotoxic substances such as cadmium.

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