

Renal toxicity of inhaled aliphatic hydrocarbons: a case report of chronic interstitial nephropathy

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ABSTRACT

We describe the case of a 58-year-old white male working as a chemical analyst in an oil refinery where he manipulated aliphatic hydrocarbons. He was referred to our Nephrology outpatient clinic with chronic kidney disease stage 4 (serum creatinine level 3.1 mg/dl [274 µmol/L]; eGFR 22 ml/min/1.73 m²). Chronic kidney disease had been detected one year earlier when the patient had a serum creatinine of 1.3 mg/dL (114.9 µmol/L) and eGFR 60 ml/min/1.73 m². After referral to us, he underwent a renal biopsy that showed chronic interstitial nephropathy, for which no aetiology has been found.

In the sixth month of Nephrology follow-up he was admitted to the emergency department of the local hospital suffering from dizziness, headaches and ataxia after a massive exposure to aliphatic hydrocarbons. On admission, he was found to have acute renal failure (serum creatinine 3.6 mg/dL [318.2 µmol/L]), attributed to acute aliphatic hydrocarbon exposure and intoxication. At this time a recommendation was made for him to change his job, and he was moved to another section where he was no longer exposed to aliphatic hydrocarbons. There was a partial recovery of acute renal failure over the next two months (serum creatinine 2.8 mg/dL [247.5 µmol/L]), with slow further improvement in renal function over the next twenty months (serum creatinine 2.5 mg/dL [221.0 µmol/L]). We therefore believe that both acute renal failure and chronic kidney disease were caused, respectively, by acute and chronic hydro-

carbon exposure, two conditions rarely reported in the literature. The role of the physician in taking an occupational history of exposure to solvents in cases of chronic kidney disease is emphasised.

Key-Words:

Aliphatic hydrocarbons, interstitial nephropathy, occupational exposure.

INTRODUCTION

Aliphatic hydrocarbons are used as solvents in many industrial processes and they are important compounds in fuel. Exposure occurs in laboratories and industries that manipulate these solvents¹. Although there has been increasing concern over occupational exposure to toxic products, something which has led to a large body of regulations, the appropriate safety and protection measures are not always taken. These practices are associated with potential health risks to the workforce.

Occupational exposure to aliphatic hydrocarbons may induce toxicity through three main kinds of contact, which are, from the more to the less frequent, inhalation, skin absorption and accidental ingestion. Aliphatic hydrocarbons are inflammable products. Vapours can be produced and irritate the upper respiratory tract and lungs. These vapours are absorbed from the lungs to the bloodstream and distributed to other parts of the body to produce additional toxic effects. Skin contact can also allow

solvent absorption and distribution to the bloodstream².

Chronic interstitial nephropathy (CIN) has been associated with a very large number of different conditions, although it is usually difficult to establish a cause-and-effect relationship.

We report a case of chronic kidney disease (CKD) associated with chronic exposure to aliphatic hydrocarbons, in which a renal biopsy showed the pathological features of CIN.

CASE REPORT

A 58-year-old white male, who had worked for four years as a chemical analyst in an oil refinery, with a 6-8 hour daily exposure to aliphatic hydrocarbons (mainly hexanes) without using the necessary protective devices (such as respirator and gloves), was referred to our outpatient clinic in August 2007 for the evaluation of progressive CKD with a serum creatinine level of 3.1 mg/dL (274 µmol/L). There was no family history of renal or other relevant diseases.

His medical background included hypertension for four years treated by his general practitioner with an angiotensin-converting enzyme (ACE) inhibitor, and a Rosai-Dorfman disease (sinus histiocytosis with massive lymphadenopathy) diagnosed in 2001 after the excision of a mass in the neck. He underwent local radiotherapy, but never chemotherapy. Since then he had been regularly followed-up in a haematology outpatient clinic where he underwent regular blood tests. In October 2006, he was found to have an elevated serum creatinine and low eGFR at 1.3 mg/dL (114.9 µmol/L) and 60 mL/min/1.73 m² respectively. Over the next eight months, creatinine levels increased progressively and eGFR decreased, to 3.1 mg/dL (274.0 µmol/L) and 22 mL/min/1.73 m², respectively, without an understandable reason. Physical examination was unremarkable.

Initial laboratory tests at the nephrology outpatient clinic showed elevated serum creatinine and low eGFR at 3.1 mg/dL (274.0 µmol/L) and 22 mL/min/1.73 m² respectively and urinalysis showed blood (++) but was negative for protein. Serum protein electrophoresis was normal. Serum complement

levels were normal. Serum immunoglobulins were within normal range. Serological testing for anti-nuclear antibodies (ANA), anti-DNA antibodies, and ANCA was unremarkable. A renal ultrasound showed no abnormality. The patient underwent a renal biopsy that showed a chronic interstitial nephropathy and tubular cell atrophy with flattened epithelial cells and tubule dilation, interstitial fibrosis, and areas of mononuclear cell infiltration in the interstitial compartment. At that time, no aetiology was found (fig 1).

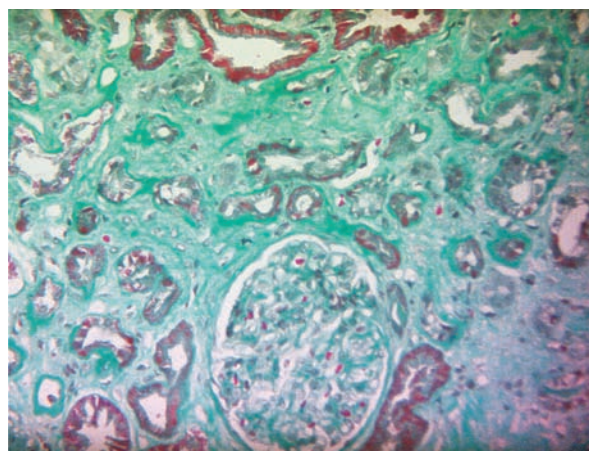


Figure 1

Renal biopsy showing interstitial fibrosis and tubular atrophy. Magnification 250 × Masson's stain.

In the sixth month of follow-up (February 2008) he was admitted to the emergency department of the local hospital suffering from dizziness, headaches and ataxia after a massive exposure to aliphatic hydrocarbons. He had worked an additional shift (eight more hours) in which he performed a new technique for the management of aliphatic hydrocarbons without using protective devices.

Laboratory analysis at admission showed an increase in serum creatinine from 2.6 mg/dL (229.8 µmol/L) to 3.6 mg/dL (318.2 µmol/L). The clinical picture was self-limiting, with a partial recovery of acute renal failure (ARF) over the next two months (serum creatinine 2.8 mg/dL [247.5 µmol/L]). Following a

medical recommendation for him to change his job, he was moved to another section where he was no longer exposed to aliphatic hydrocarbons. In the following twenty months there was a slight improvement in renal function, with serum creatinine falling to 2.5 mg/dL [221.0 μ mol/L]).

DISCUSSION

Industrial solvents are an indispensable ingredient of modern living. An association between hydrocarbon exposure and glomerulonephritis was reported as early as 1894³. Over the last 15 years, experimental data⁴, case reports⁵, case-control studies⁶⁻⁸, and epidemiological data⁹⁻¹² have documented the acute and chronic effects of solvents on the kidney, suggesting that solvents are causing or exacerbating a variety of kidney diseases, including acute kidney injury, chronic glomerulonephritis and end-stage renal disease¹³. Although two recently published epidemiological studies have shown conflicting results^{14,15}, these discrepancies may be explained by the differential detrimental effects of different types of solvents on the kidney.

Studies in experimental animal models evaluating the toxic effects of hydrocarbon exposure on the kidney have mainly shown various degrees of tubular damage⁴. Acute tubular necrosis is one of the histopathological changes that has been reported in humans¹⁴, and is most likely to be related to the direct effect of the solvent or its toxic metabolites. Chronic tubulointerstitial nephropathy after long-term occupational exposure to aliphatic hydrocarbons has, however, never been previously reported. In our patient we looked for numerous causes but found no explanation other than aliphatic hydrocarbons exposure to explain this nephropathy.

Chronic tubulointerstitial diseases of the kidney encompass diverse aetiologies and pathophysiological processes. Many forms of tubulointerstitial injury involve exposure to drugs or other nephrotoxic agents. The chronic form is an insidious disease and most probably represents the common final pattern of the kidney to a variety of insults and agents. Hypertension is common but not universal. Clinical investigations may show modest elevation in serum creatinine and evidence of tubular dysfunction. Proteinuria is usually mild; often less than 1 g/24 h. A

detailed clinical history must be performed to reach an aetiological diagnosis.

It may be very difficult to establish a cause-effect relationship in occupational exposures, because there are many confounding factors. Our patient had a Rosai-Dorfman disease, a lymphoproliferative disease characterised by formation of mixed polyclonal lymphohistiocytes. It commonly presents as massive, painless, bilateral lymph node enlargement in the neck with fevers. Sites other than the lymph nodes are rarely involved. These include the central nervous system, eyes, upper respiratory tract, skin, and head and neck region. Interestingly, the spleen and bone marrow are spared, and the kidneys are never involved.

In this case, a dose-response relationship was observed. Additionally, two facts point to the association of aliphatic hydrocarbons and renal disease. Firstly, acute massive exposure to aliphatic hydrocarbons was associated with acute renal failure, and, when the exposure was discontinued, renal function immediately improved. Secondly, chronic renal insufficiency due to chronic tubulointerstitial nephropathy was detected after one year's exposure to aliphatic hydrocarbons. While the patient maintained chronic exposure to aliphatic hydrocarbons, renal function worsened progressively over an eight-month period. When aliphatic hydrocarbons exposure was discontinued, patient maintained stable renal function over the next twenty months. A temporal relationship was thus observed between aliphatic hydrocarbons exposure and acute and chronic renal disease. Apparently the patient worked predominantly with hexanes, which are not known to be toxic to the kidney. However, volatile hydrocarbons are purified by distillation, but as raw oil is composed of thousands of different hydrocarbons, many of which have a similar boiling point, it is difficult to obtain a pure hydrocarbon. Therefore, toxic effects in the kidney may be caused by one of the impurities.

Because patients may not know the risks of their occupational exposure, some exposures to nephrotoxins may remain unnoticed. This case emphasises the importance of taking an occupational history of exposures to solvents in patients with CKD of uncertain aetiology.

Conflict of interest statement. None declared.

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