Stonemason’s systemic vasculitis: three cases and a dilemma

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Keywords: silica; stonemasons; systemic vasculitis

Introduction

There is an established link between silica exposure and the development of systemic vasculitis. There is no clear quantification of the risk of exposure, or how to protect workers against it. We report three cases of systemic vasculitis from similar workplaces and a dilemma relating to the son of one of the cases.

Case 1

A 37-year-old man presented to his GP in July 1987 complaining of a 1-month history of a blocked nose and oral ulceration. He had worked as a quarryman for several years, often in the same quarry as cases 2 and 3. During this time, he was exposed to dust from silica-rich sandstone. A nasal biopsy showed ulceration consistent with Wegener’s granulomatosis. He had dipstick haematuria and proteinuria. cANCA was positive at 1:80; serum urea and creatinine were normal. A renal biopsy was normal to light microscopy, with negative immunofluorescence, but showed mesangial proliferative changes on electron microscopy. Treatment was started with daily oral prednisolone 60 mg and cyclophosphamide 150 mg. The immunosuppression was tailed over the next year and renal function remained normal. Treatment was discontinued after 24 months and he has remained in remission for the last 13 years. He has continued to work as a quarryman in a wide range of quarries in North East England. Some of these quarries contain silica-rich stone and others are silica free.

Case 2

A 42-year-old man presented to his local hospital in January 1994 complaining of pleuritic chest pain. He had worked as a stonemason for >10 years and had frequently been exposed to dust from silica-rich sandstone. Serum creatinine was 320 μmol/l. p-ANCA was positive at 1:80. A renal biopsy showed crescentic nephritis with negative immunofluorescence. He was treated with three doses of methylprednisolone, intravenous cyclophosphamide (0.6 g/m²) and plasma exchange. Although serum creatinine fell to 260 μmol/l, there was a subsequent gradual rise and haemodialysis was started 14 months after presentation. He received a cadaveric renal transplant in August 1998. He has not returned to his previous occupation or been exposed to silica again.

Case 3

A 31-year-old man was admitted to his local hospital in January 2002 complaining of shortness of breath and calf swelling. He had worked as a stonemason for 14 years in the same quarry as case 2, with similar exposure to dust from silica-rich sandstone. He is the nephew of the wife of case 2. A CT chest showed evidence of pulmonary embolus and hilar lymphadenopathy. He was started on warfarin and referred for mediastinoscopy. On admission for that procedure, serum creatinine was 350 μmol/l. pANCA was positive at 1:80. A renal biopsy showed pauci immune crescent glomerulonephritis. The patient was started on intravenous methyl prednisolone and oral cyclophosphamide (2.5 mg/kg). His renal function worsened and he became dialysis dependent 6 months after presentation.

Case 4

A 25-year-old man, son of case 2 and cousin of case 3, is currently well. He works as a stonemason in the same...
quarry as his father, with similar silica exposure. He has 3-monthly checks on blood pressure and urinalysis. Alternative employment would be difficult to find and he is reluctant to leave his current job.

Discussion

There is an increasingly well documented association between silica exposure and renal disease. Cohort studies of 2412 gold miners [1] and 2980 ceramic industry workers [2] demonstrated an increased risk of developing end-stage renal failure (ESRF). The risk was greatest in gold miners for ESRF caused by glomerulonephritis or interstitial nephritis, for which the standardized incidence ratio was 4.22, whereas in ceramic industry workers there was a 3-fold greater than expected incidence of ESRF. Case–control studies also support the association. For example, Nuysts et al. [3] found that occupational exposure to silicon-containing compounds increased the risk of developing chronic renal failure; odds ratio (OR) 2.51 (1.37–4.60).

A specific link between ANCA-associated systemic vasculitis (AASV) and silica exposure has also been suggested. Gregorini et al. [4] studied a subset of 16 patients with ANCA-positive glomerulonephritis. An occupational history of silica exposure was taken by an industrial hygienist. The cases were much more likely to have been exposed than the controls; OR 14.0, P < 0.001. Hogan et al. [5] looked at occupational exposure in 65 cases of AASV with biopsy-proven renal involvement. Occupational exposure was identified by a self-administered questionnaire. Silica dust exposure was reported in 46% of cases compared with 20% of controls (P = 0.001). The risk estimate for cANCA disease was OR 4.0 (P = 0.013) and for pANCA OR 7.0 (P = 0.069).

The risk of developing renal disease appears to be linked to the amount and duration of silica exposure. One study calculated risk estimates for different jobs involving silica exposure. Hogan et al. [5] found that sandblasting carried the highest risk, more than brick, foundry, cement and sand workers. Calvert et al. [1] showed that the length of exposure was a risk factor for developing end-stage renal disease.

The way in which silica causes renal damage is unknown, but in vitro studies of the effects of silica particles have shown potent activation of macrophages, monocytes and lymphocytes [6]. It seems likely that the development of renal disease related to silica exposure is mediated by abnormal immune system activation rather than a direct toxic effect.

As with other autoimmune diseases, it is probable that certain genotypes predispose to the development of AASV. Several studies looking at immunorelevant genes in Wegener’s granulomatosis and AASV have shown links with myeloperoxidase (MPO) promoter polymorphism [7], interleukin-10 (IL-10) [8], Fcγ receptors [9] and CD18 gene expression [10]. No specific genetic risk has been identified for silica-related renal disease.

It seems likely that the three cases presented here have silica-related AASV. Cases 2 and 3 clearly had AASV and both shared a long history of exposure to silica-rich sandstone in the same quarry. Case 1 had AASV diagnosed on clinical findings and a positive cANCA without specific histological support. He worked in the same quarry as cases 2 and 3 prior to his illness, but had less consistent exposure to silica. He continues to work in quarries as a driver and only has low exposure to silica.

Over the past 15 years, a total of ~50 masons have been employed in the quarries where our cases have worked. Precise exposure records are not kept. Masons are advised how to minimize the pulmonary risks of silica exposure and offered protective masks. Compliance with this is variable, but there have been no recent cases of silicosis.

Perhaps unsurprisingly, the wife of case 2 and aunt of case 3 has been very worried about her son, case 4. She would like to know his chance of developing AASV, and whether or not continuing his current job increases those chances. We have said that we believe him to be at an unquantifiable increased risk of developing AASV because of his environmental exposure, and the possibility of a genetic predisposition. We have advised him to comply fully with all protective measures, and have taught him to check his urine regularly for dipstick haematuria and proteinuria. We have not advised regular ANCA checks as we have tried to avoid visits to the doctor, and ANCA is often low or negative in limited or early disease. His GP and occupational health doctor are aware of the family history and risk of developing AASV. We feel unable to give strong advice to him to leave his job, especially if the only other option is unemployment. While there is documented evidence that links silica exposure to renal disease, it is not a recognized industrial disease and no compensation is available. We have written to the UK Industrial Advisory Board regarding the likely renal effects of silica exposure.

Conflict of interest statement. None declared.

References


Received for publication: 24.2.03
Accepted in revised form: 22.9.03