*Project S.E.N.S.O.R. News

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Kidney Disease and Silicosis

Workers exposed to silica are at risk of developing a number of conditions in addition to silicosis. These conditions include: connective tissue diseases (rheumatoid arthritis, sclerodema, systemic lupus erythematosus), emphysema, kidney disease, lung cancer and tuberculosis. We have recently reviewed the medical records of 583 Michigan residents with confirmed silicosis to determine the prevalence of kidney disease in this population. We looked for any mention of kidney disease in the patients' hospitalization records, including the admitting history and physical and discharge summary. We also abstracted all creatinine values from the 283 individuals whose medical records included laboratory results.

Silica exposure has been associated with both glomerular and tubular kidney dysfunction (1-16). Data supporting the association includes case reports (1,4,10,14-16), cross sectional studies of tubular function (2,9,11,12), pathological studies (8,17), positive tests for antineutrophil cytoplasmic antibody (ANCA) (6), epidemiological studies of end stage renal disease (3,18), and case control studies of ANCA positive Wegener's Granulomatosis (5,13).

Case Report

A white male in his 60's worked 28 years, from 1965 to 1993, in a foundry. He had symptoms of chronic productive cough, dyspnea and fatigue. He had held multiple jobs in the foundry including making molds, chipping and sandblasting. He never smoked cigarettes. He had a negative skin test for tuberculosis. He did not apply for workers' compensation. His chest x-ray showed r/u type opacities in the upper and mid zones with a profusion of 3/3 per the International Labor Organization's (ILO) criteria. His FVC was 1.46 liters, 29% of predicted, and his FEV_1 was 1.10 liters, 28% of predicted. His FEV_1/FVC ratio was 75%.

In 1993 he was diagnosed with anti-neutrophil cytoplasmic antibody positive vasculitis and nephritis. A kidney biopsy specimen showed two portions of tissue containing a total of 2 to 4 glomeruli. The interpretation was interstitial fibrosis, mild interstitial chronic inflammation, and varying sclerosing features. Immunofluorescent histology was negative for IgG, IgA, IgM, Clq, C4, albumin, fibrinogen, and kappa and lambda light chains. There was 1 + diffuse coarse granular staining of walls of globally sclerotic glomeruli for C3.

The final interpretation after electron microscopy was ischemic nephropathy associated with hyaline arteriolar sclerosis, (moderate to focal marked); focal immune complex mesangiopathic changes of uncertain etiology (an IgA nephropathy cannot be excluded); and tubulointerstitial inflammation and scarring. His blood urea nitrogen level was 50 mg/dl and creatinine 2.4 mg/dl. He took prednisone daily.

Table I shows a statistically non significant increasing prevalence of kidney disease and serum creatinine levels > 1.5 mg/dl with increasing age for Michigan silicotics. We found that approximately 10% of the Michigan registry silicotics younger than age 50 had chronic kidney disease and that 33% had serum creatinine levels > 1.5 mg/dl.

We compared the prevalence of serum creatinine greater than 1.5 mg/dl within age and race strata to results in the general population based on the third National Health and Nutrition Examination Survey data (20). The individuals with silicosis had a significant increase in the prevalence of elevated serum creatinine as compared with age, race, and gender matched controls from the general population (Table II).

However, we did not find any association between our two surrogate measures of silica exposure

(profusion of scarring on chest x-ray and duration of exposure to silica) and prevalence of elevated serum creatinine and/or presence of kidney disease. Additionally, individuals with kidney disease or elevated serum creatinine level were less likely to have sandblasted (OR= .49, 95% CL .25-93), a work practice which causes particularly high levels of exposure, and no more likely to have applied for workers' compensation (OR = 1.07, 95% CL .65-1.76), a possible marker of severity of silicosis.

Two possible mechanisms have been proposed for silica's effect on the kidney: 1) a direct nephrotoxic effect; and 2) an adjuvant effect to the immune system which evolves into an autoimmune renal disease (21). The absence of an association in our data between surrogates of exposure (ie. duration and x-ray severity) do not support a direct dose-related nephrotoxic effect of silica. The lack of an association with exposure, the known increased prevalence of positive tests for anti-nuclear antibodies and rheumatoid factor in individuals with silicosis as well as the increased prevalence of clinical connective disease among silicotics, a case report with positive immunofluorescence studies showing diffuse IgA and C3 mesangial deposits (22) and the studies associating Wegener's granulomatosis with silica exposure all support the autoimmune hypothesis. In a previous study of this same cohort we found an increase in connective tissue disease which again was not associated with duration of exposure or severity of disease (22).

On the other hand our case report and others have reported negative immunofluorescent findings on kidney biopsy (15). These findings coupled with the presence of a dose response effect in some studies (3,12,18) and the presence of acute renal failure after massive exposure (4) support a direct nephrotoxic effect of silica. There is no reason why silica cannot be capable of causing kidney disease by both mechanisms. Whatever the mechanism, chronic kidney disease should be considered a potential complication in patients with silicosis. The full results of this analysis are scheduled to be published in the journal *Nephron*.

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Table I. Prevalence of Kidney Disease and/or Serum Creatinine (CR) >1.5 mg/dl by Age: Michigan Silicosis Registry, 1987-1995

	Kidney Disease		CR >1.5		Either Kidney Disease or CR >1.5	
Age	#	%	#	%	#	%
< 50	0	0	2	50.0	2	12.5
50-59	1	2.2	1	9.1	1	2.2
60-69	8	6.4	13	26.0	18	14.4
70-79	19	10.3	27	30.3	31	16.8
≥80	28	13.2	49	38.0	57	26.9
Total	56	9.6	92	32.5	109	18.7
	(X^2=.78, p=.377)		(X^2=3.22, p=.073)		(X^2=16.43, p=.00005)	

Table II. Percent of Individuals with Silicosis, 1987-1995 with Creatinine >1.5mg/dl in Comparison with Results from NHANES III, 1988-1994, by Race and Age

	Age Range (years)				
	<50	50-59	60-69	70-79	≥80
White					
Silicosis	10.0%	0	20.8%	30.4%	35.9%
Control	0.6%	2.3%	5.1%	13.4%	22.7%
African American					
Silicosis	33.3%	25.0%	28.0%	31.0%	39.7%
Control	2.2%	9.2%	19.8%	23.4%	27.7%

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