**CLINICAL VIGNETTE**

# Silicosis and Renal Failure in a Kitchen Fabricator

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***Case***

A 41-year-old male with no known past medical history was referred to the emergency department by his recently established primary care doctor for fatigue and bilateral leg swelling for the past week. He was recently started on losartan 40mg and hydrochlorothiazide for hypertension, but no other medications or drug abuse. He was a former smoker; 1.5 pack year and quit 5 years ago. He immigrated to the United States 28 years ago from Mexico and previously worked as a kitchen fabricator for 18 years. Admission vital signs were significant for hypertension to 166/87 mmHg, but were otherwise within normal limits. Physical exam revealed conjunctival pallor, slightly increased work of breathing, bibasilar crackles, and bilateral pitting edema to the level of the ankles. Initial labs were significant for anemia, Hgb 5.6 g/dL, Hct 16.9%, leukocytosis 14.5 K/cumm, hyperkalemia 6.0 mmol/L, CO2 9 mmol/L, BUN >200 mg/dL, Creatinine 24.29 mg/dL, Ca 7.6 mg/dL, phosphorus 20.8 mg/dL, Uric acid 11.8, and BNP 2619 pg/mL. CT of the chest, abdomen, and pelvis was obtained due to concern for tumor lysis syndrome. It showed reticulonodular, tree-in-bud, and nodular opacities throughout the bilateral lung fields, prominent bilateral mediastinal lymph nodes, diffuse anasarca, but no overt malignancy.

The patient was started on urgent dialysis and given 1 unit packed RBC transfusion along with empiric antibiotics. Extensive infectious workup with procalcitonin, urine analysis, blood cultures, induced sputum bacterial and AFB cultures, HIV, hepatitis B/C, RPR, QuantiFERON-gold, and other fungal etiologies (histoplasmosis, cryptococcus, coccidiomycosis, aspergillus) were all negative. Labs to evaluate chronic kidney disease and vasculitis were only significant for urine protein/Cr ratio of 16.5, elevated ESR 120 mm/hr and CRP 95.3 mg/L, and positive ANA titer 1:160. Negative studies including anti-smith, anti-dsDNA, anti-cardiolipin, anti-phospholipid, and anti-GBM antibodies, along with SSA/SSB, ANCA, Complement 3 and 4, free kappa/lambda ratio, and SPEP/UPEP. The patient underwent bronchoscopy with transbronchial biopsy and bronchoalveolar lavage (BAL), which were negative for malignant cells or microorganisms, but showed lung parenchyma with small patchy nodules of histiocytes and rare fibroblasts with black particles that stained positive for iron, compatible with silicosis. The patient completed an empiric course of antibiotics, and his leg swelling improved with dialysis. He was discharged home with a tunneled hemodialysis catheter for outpatient dialysis, but was unfortunately lost to follow-up after 1 month.

***Discussion***

This patient with silicosis and renal failure presented with volume overload. Silicosis is a fibrotic lung disease caused by inhalation of silica dust. It is most associated with occupational exposures, and has been called various names such as “miners’ phthisis,” “mason’s disease,” “grinders’ asthma,” and “stonecutters’ disease.[1]” Since the first report of artificial stone-related silicosis in Israel in 2010, artificial stone cutting has been increasingly recognized as an occupational hazard, and has been so declared by the Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH).[2,3] Kitchen fabricators such as our patient often process artificial stones that contain high amounts of silica, usually over 90%. These stones are turned into kitchen countertops, releasing hazardous levels of very small, crystalline silica dust particles that can be inhaled by workers.[2] Silica’s mechanism of toxicity is thought to be from its interaction with aqueous media, generating free radicals that injures pulmonary cells, causing an inflammatory cascade that ultimately results in fibrosis.[4]

Silicosis has a variety of clinical and pathological presentations. Three commonly described forms include acute, accelerated, and chronic silicosis. Acute silicosis, also called acute silicoproteinosis, is a rare form of silicosis characterized by proteinaceous material filling alveolar spaces that stain positive with periodic acid-Schiff reagent mimicking pulmonary alveolar proteinosis.[5] Historically, specific occupations associated with the development of acute silicosis including silica flour processing, tombstone sandblasting, and surface drilling.[1] Symptoms such as dyspnea, cough, weight loss and fatigue usually develop within a few weeks to years after exposure to high concentration of broken/fractured silica particles. Currently, there is no specific treatment for acute silicosis besides supportive care and exposure avoidance. Experimental treatments with systemic glucocorticoids and whole lung lavage have been attempted in case reports, but the overall prognosis of acute silicosis is poor with case series recording an average life expectancy of 7.5 months after the onset of symptoms.[5]

Chronic silicosis is the most common form of silicosis that develops after decades of repeated exposure. Clinical presentation is variable in chronic silicosis. Patients can be asymptomatic with only radiographic changes, or have chronic cough and dyspnea on exertion. Patients can also develop progressive massive fibrosis (PMF), a debilitating subset of the disease that is prone to mycobacterial infections, spontaneous pneumo-

thoraces, and fatal respiratory failure. Chest radiographs of chronic silicosis are distinguished by large upper lobe opacities with small diffuse nodular lesions (<10mm). PMF occurs when the nodular lesions enlarge to >10mm.[6] Pulmonary function including FEV1, FEV1/FVC ratio, and DLCO all decrease with worsening radiographic findings.[1] Diagnosis of chronic silicosis is clinical based on history of exposure, chest imaging, and absence of alternative diagnosis. Like acute silicosis, the treatment of chronic silicosis is mainly supportive with emphasis on limiting further exposure. Lung transplant can be considered, but data on survival outcomes on post-transplant patients are conflicting.[2]

A third form of silicosis has been described called accelerated silicosis. It can present with similar symptoms and radiographic findings compared to chronic silicosis, however, accelerated silicosis is associated with several autoimmune disorders with a shorter silica exposure time frame of 5 to 15 years.[1] Our patient had 18 years of silica exposure via artificial stone processing and mild pulmonary symptoms, which is more compatible with chronic silicosis. His imaging did not show large nodular lesions that would make one suspect PMF, although concurrent volume overload did confound the picture. Elevated inflammatory markers and positive ANA in the setting of renal failure were suspicious for underlying autoimmune etiologies such as lupus or granulomatosis with polyangiitis. However, the otherwise negative autoimmune testing, lack of systemic symptoms, and bronchoscopy results were inconsistent with other systemic autoimmune processes.

Interestingly, there have been multiple reports of association between silicosis and nephropathy in the medical literature. A 1999 retrospective cohort study conducted by Michigan State University reported 10% of 583 individuals with silicosis, with chronic kidney disease, and 33% of the 283 patients with lab results with serum creatinine levels greater than 1.5mg/dl regardless of exposure duration.[7] In another case-control study of 325 men with ESRD, the risk of ESRD was significantly related to occupational silica exposure (OR=1.67) especially in foundries, brick factories, and sandblasting. In Lazio, Italy, a cohort of 2980 male ceramic workers were detected to have higher incidence of ESRD compared to the general population (Observed/Expected=3.21; 95% CI: 1.17-6.98).[8] The pathogenesis of kidney injury in silicosis is still unclear. Two proposed mechanisms include direct nephrotoxic effect of crystalline silica, and an autoimmune process involving the interaction of silica particles with the immune system leading to the formation of immune complexes deposited in the glomerulus causing glomerulonephritis. The etiology of renal failure in our case is unclear. There was consideration of renal biopsy, but nephrology felt that the patient's progressive renal failure was most likely from poorly controlled hypertension. Kidney biopsy was unlikely to change dialysis management.

### *Conclusion*

Silicosis has been a long-recognized disease associated with occupational exposures. Crystalline silica inhalation is associated with a range of pulmonary pathologies from acute to chronic silicosis. There is also increasing evidence that silicosis is associated with renal dysfunction via direct toxicity and glomerular immune complex deposition. One occupation at high risk of crystalline silica exposure is the processing of artificial stones used in the fabrication of kitchen and bathroom countertops that has been growing in popularity. Since treatment options for silicosis are limited, exposure prevention is critical. Patients with respiratory symptoms and/or suspicious imaging findings should be screened for occupational exposures, and further exposure should be avoided or minimized.

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