

Abstract Submission No. : 9011

Three cases of silicosis with mediastinal lymphadenopathy complicated with membranous nephropathy or membranoproliferative glomerulonephritis

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Cases: Three men with silicosis and mediastinal lymphadenopathy presented with proteinuria and worsening serum creatinine. Renal biopsies were performed. Their background and biopsy findings are summarized in Table 1.

Discussion: Silicosis, asthma and COPD are major occupational respiratory diseases in workers with silica exposure (Park SY, et al. J Korean Med Sci. 2014.). RA associated with silicosis (Caplan's syndrome) is believed to be caused by inflammasome activation by crystalline silica phagocytosed by macrophages (Leung CC, et al. Lancet. 2012.). Past literature (Osorio AM, et al. AJKD. 1987.) and our findings suggest that various patterns of immune complex deposition in the glomeruli may cause membranous nephropathy or membranoproliferative glomerulonephritis in silicosis patients even decades after silica exposure. Silicosis, mediastinal lymphadenopathy and proliferative glomerulonephritis may compose a syndrome. These findings may help investigate the etiology of increased membranous nephropathy in smokers (Yamaguchi M, et al. PLOS ONE. 2014.) or in residents in air-polluted areas (Xu X, et al. JASN. 2016.).

Table 1. Summary of the cases


KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

	Case 1	Case 2	Case 3	
Clinical presentation	Worsening renal function	Subacute-onset nephrotic syndrome		
Age, sex	61-year-old man	71-year-old man	71-year-old man	
Profession	Stonemason, 40 years	N/A	Cement worker, 40 years	
Lung disease	Silicosis	Silicosis, asthma (50 y/o)	Silicosis, COPD (63 y/o)	
Lymphadenopathy	Hilar, supraclavicular	Mediastinal	Mediastinal	
Comorbid disease	Hypertension	RA (69 y/o), cerebral infarction	RA (60 y/o), hypertension	
Proteinuria	1.0 gram/day	9.7 grams/day	8.0 grams/day	
Hematuria	Negative	Positive: (2+)	Positive: (3+)	
Serum creatinine	5.1 mg/dL	1.5 mg/dL	1.2 mg/dL	
Renal biopsy	Light microscopy	Spike, double contour, atherosclerosis	Minimal change	Double contour, lobulation, mesangial proliferation
	Fluorescence microscopy	Granular IgG on GBM, C3 on mesangium and GBM	Granular IgG on GBM (IgG1 > IgG4 ≥ IgG2), C3 on GBM	Granular IgG on GBM (IgG4 >> IgG1 > IgG3), C3 on mesangium and GBM
	Electron microscopy	Intramembranous > subepithelial > mesangial deposits	Subepithelial deposits	Subepithelial, subendothelial > intramembranous, mesangial deposits

* Abbreviations: N/A, not available; COPD, chronic obstructive pulmonary disease; RA, rheumatoid arthritis; IgG, immunoglobulin G; GBM, glomerular basement membrane.

* In case 1, supraclavicular lymph node biopsy revealed many epithelioid cells and enclosed silica crystals.

* In case 3, improvement in proteinuria, hematuria, and ground glass opacity were observed after steroid therapy.