Case Report

Lupus-like autoimmune disease associated with silicosis

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Introduction

Major occupational exposures to silica occur in the mining, stone-cutting, and abrasives industries [1,2]. Estimates of the total number of exposed workers in the US today range from 1.2 to 3 million people [2]. Although prolonged exposure to silica has long been associated with pulmonary pathology, a growing body of evidence suggests that the lung is not the only organ affected by silicosis. Several recent case reports have documented a relationship between the development of pneumoconiosis and systemic vasculitis [3-6]. We now report a case of end-stage renal disease occurring within the context of a silicosis-induced connective-tissue disorder similar in many respects to systemic lupus erythematosus.

Case report

A 58-year-old caucasion male was referred to our institution for evaluation of new-onset renal insufficiency. He complained only of oliguria and mild exertional dyspnoea. As an employee of the chemical industry, he had been involved in the manufacture of abrasive cleaners for 15 years. Review of systems was positive only for a 30-lb weight loss over the preceding year. His presenting creatinine clearance was 17 ml/min. Physical examination revealed an anaemic, ill-appearing gentleman weighing 60 kg. His blood pressure was 160/95. Urinalysis revealed 3+ proteinuria and 11–20 r.b.cs; no casts were observed and the rest of the urinalysis was unremarkable. Ultrasound demonstrated normal size kidneys and there was no evidence of hydronephrosis. Renal biopsy showed both glomerulosclerosis and chronic interstitial nephritis (Figure 1). Congo-red staining for amyloid was negative. Immunofluorescence was positive for the granular deposition of C3, fibrin, and IgM peripherally. No IgG deposits were detected.

Despite conservative management, the patient progressed to end-stage renal disease within 4 months. Laboratory findings at that time were as follows: haematocrit 27%, leucocyte count 3800/µl, platelet count 100 000/µl. Serum calcium, phosphate, sodium, potassium, and chloride were all within normal limits. Serum creatinine had increased to 14.9 mg/dl, and albumin was 2.5 g/dl. Rheumatological studies demonstrated an elevated sedimentation rate (>100 mm/h) and an antinuclear antibody (ANA) titre of 1:2560. Serological assays were also positive for anti-Ro, anti-La, and anticardiolipin antibodies. Antimyeloperoxidase and perinuclear antineutrophil cytoplasmic antibodies (P-ANCA) were present. C-ANCA was absent. Other negative serological markers included rheumatoid factor, anti-Smith, anti-mitochondrial and anti-DNA antibodies. Syphilis and hepatitis serologies were also unremarkable, and all complement levels were within normal limits.

Prior to placement of a peritoneal dialysis catheter, a chest X-ray was obtained which revealed multiple pulmonary opacities and bilateral pleural effusions (Figure 2). Thoracentesis yielded a sterile haemorrhagic exudate. Bronchoscopy and open lung biopsy revealed pneumoconiosis with extensive pulmonary...
fibrosis and multiple well-organized granulomata (Figure 3).
The postoperative course of this patient was long and complicated. Following thoracotomy, he developed generalized erythroderma and a gradually progressive exfoliative dermatitis (Figure 4). These skin changes were accompanied by fevers, worsening pancytopenia, and the production of voluminous, haem-positive, maroon-coloured stool. Skin Bi at that time revealed the presence of leukocytoclastic vasculitis (Figure 5). Throughout his hospital stay this patient required maintenance on haemodialysis as well as multiple blood and platelet transfusions, raising the possibility of a transfusion-related graft-versus-host disease. However, HLA typing of both skin and peripheral blood leukocytes showed no exogenous DR subtypes, making such a diagnosis unlikely.
Unfortunately, the patient's course was further complicated by enterococcal peritonitis, catheter-related sepsicaemia, and an episode of bacterial endocarditis which left him with aortic valve insufficiency. Because
of his predisposition to recurrent infection occurring in the context of a proliferative exfoliative dermatitis, the possible diagnosis of cutaneous T-cell lymphoma (CTCL) was also entertained. Although some lymphocytes on his peripheral smear did appear to contain cerebriform nucei, a Sezary cell preparation from his blood buffy coat was negative. Furthermore, T-cell receptor gene rearrangement studies showed no clonality, essentially ruling out a diagnosis of CTCL. Bone-marrow biopsy was hypercellular, but otherwise normal with trilinear haematopoiesis (not shown).

Discussion

Recent case reports have suggested a link between prolonged exposure to silica and various forms of connective tissue disease [3–6]. The coexistence of pneumoconiosis with the serological evidence of an autoimmune process is not uncommon [5]. Estimates of the prevalence of an elevated antinuclear antibody titre specifically accompanying silicosis have ranged from 26 to 44% [7,8]. Perhaps this association is the result of an immune response evoked by destructured components of the granulomatous silicotic nodules.

The finding of antinuclear antibodies in our patient's serum suggests the presence of a lupus-like autoimmune process. However, anti-DNA and anti-Smith antibodies were absent, making the diagnosis of systemic lupus erythematosus less plausible [2,5]. The presence of antineutrophil cytoplasmic antibodies (P-ANCA) suggest the diagnosis of Wegener's granulomatosis. In fact, a recent case report has implicated this disease as causative in the declining renal function observed in a patient known to have silicotic pulmonary nodules [3]. Although our patient's open-lung biopsy did demonstrate the presence of granuloma, his renal biopsy did not. Furthermore, his serological analysis was negative for C-ANCA, a marker estimated to be 90% sensitive and 95% specific for the diagnosis of Wegener's granulomatosis. The presence of anti-Ro and anti-La antibodies suggests an alternative diagnosis of Sjögren's syndrome; however, our patient was remarkably negative for the common signs and symptoms of this disease. Although he did not meet strict diagnostic criteria for any single rheumatological disease, a lupus-like autoimmune process had clearly left him with end-stage renal disease.

The renal lesions documented in systemic lupus erythematosus are characteristically pleomorphic. Four major histological groupings are recognized: minimal lesions, proliferative lupus nephritis (focal and diffuse), membranous lupus nephritis, and chronic sclerosing nephritis [9,10]. Our patient's renal pathology showed changes most consistent with the latter grouping. Interestingly, though, sclerotic glomeruli were not the only outstanding feature of his renal biopsy; there was a significant amount of lymphocytic infiltration into the mesangium as well. Whether this observation reflects the presence of a second discrete pathogenic process or a parenchymal extension of the first is unknown.

Previous investigators have proposed the coexistence of two distinct pathogenetic mechanisms responsible for the collective histological changes seen in the nephritis of systemic lupus [9]. While the diffuse sclerotic changes are probably the result of immune-complex deposition, current evidence suggests that focal lesions result from thrombosis-induced intracapillary necrosis and aneurysmal dilatation of the capillary walls [11]. Formation of these microangiopathic thromboses have been linked to the presence of autoantibodies with high affinity for negatively charged phospholipids [12], such as the anticardiolipin antibodies noted to be present in the serum of our patient.

Evidence has suggested that bolus doses of intravenous methylprednisolone, with or without alkylating agents, can be helpful in slowing the progression of proliferative lupus nephritis [10]. Although our patient had renal pathology which had clearly advanced beyond any chance of intervention, he was given a trial of glucocorticoids in an effort to curtail the progression of his pancytopenia and profound exfoliative dermatitis. During an infection-free period he was started on high-dose intravenous methylprednisolone which resulted in remarkable symptomatic improvement. It was hypothesized that this patient's lupus-like autoimmune disease was related to his long occupational exposure to silica. At present he remains clinically stable on a low maintenance dose of oral glucocorticoids, and his end-stage renal disease is being managed by routine haemodialysis.

As this and similar case reports continue to appear in the renal and pulmonary literature, it becomes increasingly evident that silicosis (more than any other form of pneumoconiosis) is associated with the induction of a systemic autoimmune process. A thorough occupational history is therefore critical in the evaluation of patients that present with otherwise unexplainable renal insufficiency.

References

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