Silica-induced Lupus Erythematosus

Sir,

Silica-induced lupus erythematosus (SLE) is a chronic multi-organ system autoimmune disease with frequent exacerbations and remissions. The pathomechanism of the disease is not yet completely understood. Based on a genetic background, disturbances of the immune regulation seem to play a major role, such as T-cell abnormalities, including T-cell cytokine network, polyclonal B cell stimulation, immune complex formation, defects in the immune complex clearance and dysregulation of apoptosis. Recently environmental factors have been discussed, such as drugs (procainamide, hydralazine, isoniazid, chlorpromazine, methyldopa, quinine diphenyl hydantoin), solvents (1) and silica (2–7).

Here we report on 4 male SLE patients with long-term silica exposure and silicosis.

CASE REPORTS

The historical, clinical and laboratory data of the 4 male SLE patients are given in Table I. They were between 46 and 63 years old, with silica exposure times between 12 and 23 years before the outbreak of SLE. All had been occupied in industry involving mining, drilling, cutting or polishing rock. The ARA criteria for SLE were fullfilled by the patients. As shown by high-resolution computer tomography, the lung was involved either as silicosis or as bibasilar fibrosis with hypertension in 2 cases and the development of antiDNA antibodies in all of them. Offending drugs or exposure to solvents could not be detected. Therapy was conducted according to the rules in idiopathic SLE with glucocorticoids and immunosuppressants and with angiotensin-converting enzyme inhibitors in 2 cases.

DISCUSSION

In the literature there are several reports on the association of lupus erythematosus (LE) with silicosis (2) or with occupational silica exposure (3, 5). In addition, Mehlhorn & Gerlach (4) and Ziegler et al. (5) found several cases in the uranium mining industry in former East Germany. In a survey of 877 male LE patients (592 SLE, 279 DLE) we only found 7 patients with silicosis out of 428 SLE patients over 40 years of age.

The respiratory system is involved in about 50% of SLE patients. Silicosis is caused by long-term inhalation of silica crystals, which form small nodules in the lung, either diffusely distributed or primarily in the upper lobes. All our patients had long-term exposure and occupations that were dangerous because of heavy silica dust concentrations.

Silica may act as an adjuvant, which increases the immune answer to foreign antigens. Hypergammaglobulinemia occurs frequently in silicosis patients (8) in association with rheumatic factors (9), immune complexes and antinuclear antibodies (10). In in vitro studies we have shown that silica activates the cytokine release from monocytes (11), adhesion molecules on endothelial cells (12) and also various functions of fibroblasts (13). In addition, oxygen radicals and peroxides

Table I. *Historical, clinical and laboratory data of 4 male silica-induced SLE patients*

Symptoms	Pat. 1	Pat. 2	Pat. 3	Pat. 4
Age (years)	51	46	63	58
SLE since	1990	1988	1993	1993
Malar rash	+	+	+	+
Discoid rash	(+)	–	+	–
Photosensitivity	++	+	(+)	++
Oral ulcers	–	+	+	–
Arthritis	+	(+)	++	++
Serositis	–	pericarditis	pleuritis	–
Renal disorder	+	–	–	+
Neurological disorder	–	–	–	(+)
Hematologic disorder	leucopenia	anemia leucopenia	anemia thrombocytopenia	–
Immunologic disorder	antiLa,Ro	antiSm	antiLa	antiphospholipid
Antinuclear antibodies	antiDNA 1:640	antiDNA 1:1600	antiDNA 1:2560	antiDNA 1:320
Hypergammaglobulinemia	+	(+)	+	+
BSR	increased	(increased)	increased	increased
Silica-exposure	17 y	12 y	23 y	19 y
Occupation	uranium hewer	cast polisher	stone-mason	uranium driller
Silicosis	+	bibasilar lungfibrosis	+	+
Offending drugs	–	–	–	–
Solvents	–	–	–	–
HLA	DR2, A1, B8	A1, B8	DR2, DR3, B8	DR2, DR3
Treatment	methylprednisolone cyclophosphamide captopril	methylprednisolone azathioprine	methylprednisolone methotrexate	methylprednisolone enalpril azathioprine

may be formed and released from macrophages. Parallels to the pathogenesis of silica-induced scleroderma are given, as observed in 111 patients in our department (14).

As silica cannot be removed from the body, its precipitating effect cannot be stopped. This indicates that the clinical course is that of classical autoimmune diseases, with progressions and remissions. The therapy has to be in line with these facts and has to be adjusted according to the criteria of the clinical activity of the disease. The best way to prevent this type of SLE is to minimize the exposure to silica.

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Centroblastic-centrocytic Lymphoma Arising at the Site of Previous Herpes Zoster Eruption

Sir,

The development of a skin disorder at the site of an unrelated, already healed disease is known as isotopic response.

We describe a patient in whom a centrocytic-centroblastic lymphoma developed at the site of a previous herpes zoster.

CASE REPORT

In 1994, a 58-year-old Caucasian man had a herpes zoster eruption on the left antero-lateral thoracic region. Three months later, asymptomatic, firm, brown-red papulonodular lesions, 0.5–2.0 cm wide, began to develop on the zoster site, where only a pigmented macule had remained (Fig. 1). Axillary lymph nodes and spleen were not palpable.

Laboratory tests, including complete blood cell counts, liver and renal function, were within normal ranges. No concurrent extracutaneous disease findings were detected by chest radiography, computerized abdominal tomography and echography.

Histopathology of a nodular lesion showed a lymphoid infiltrate in the papillary and reticular dermis without epidermotropism, mainly composed of a mixed centrocytic/centroblastic population with a conspicuous follicular pattern. Collagen bundles were in part dissociated by the infiltrate. Immunohistochemically, most of the lymphoid cells stained with anti-CD20 monoclonal antibodies and a few of them with anti-CD3 monoclonal antibodies. Immunocytochemistry showed a monoclonal proliferation of cells staining for mu and kappa chains.

Treatment with natural interferon alpha (3 MU three times a week IM) was initiated, and the lesions cleared completely in 8 months. The drug was then stopped and, 3 months later, the tumour relapsed in the same area. The lesions partly cleared after a second course of interferon therapy at the same dosage.

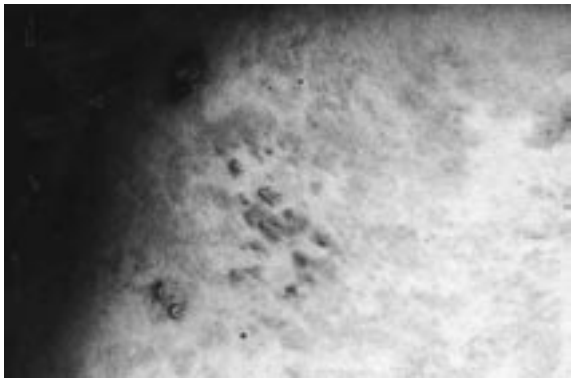

Fig. 1. Papulo-nodular lesions surrounded by annular erythema on the left antero-lateral thoracic region.

DISCUSSION

The term isotopic response refers the occurrence of a new skin disorder at the site of another one, already healed and unre-