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Case Report

Solvent induced systemic sclerosis: A case report with literature review

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Abstract
Systemic sclerosis is an important autoimmune disease. Sclerodermatous skin changes and systemic sclerosis have been reported to occur as a result of occupational exposure with several different organic solvents. We describe a 56-year-old man who developed systemic sclerosis with skin and renal involvement after working for 20 years in a tire industry, where he had prolonged exposure to toluene and benzene by inhalation. Tire building has some process such as mixing, blender, calendaring, extruding and vulcanization. Solvents such as benzene and toluene produced during these procedure specially vulcanization. Our patient had worked in a no ventilated workplace, also the exposure level of benzene and toluene was more than threshold exposure limit. He mentioned the same symptoms (Raynaud's phenomenon) in one of his co workers that quitted his work.

INTRODUCTION

Systemic sclerosis is a multisystem disorder characterized by association of vascular abnormalities, connective tissue sclerosis, atrophy, and auto antibodies [1-4]. It appears that female to male ratio is between 3 and 6 [5]. In men, the condition appears to be more common among those who work in dusty trades [6]. Research has recognized that the cause of this disease is strongly linked to a combination of genetic factor, hormonal events and external triggers. Specifically occupational exposure to various chemicals including vinyl chloride, silica dust, epoxy resin and solvents has been described as a potential provoking factor of systemic sclerosis and scleroderma like disorders. The first case report of systemic sclerosis (SSc) associated with solvent use was in 1957 [7-8]. A number of cases have reported include aliphatic hydrocarbons (vinyl chloride, perchloroethylene, and trichloroethylene) and 20 cases about aromatic hydrocarbons such as benzene, toluene, xylene and diesel [9-10].

Occupational exposures linked with SSc include polyvinyl chloride, epoxy resins, and aromatic hydrocarbons including toluene and trichloroethylene [11]. Organic solvents penetrate the skin, can be inhaled, and may produce metabolic changes in many organs, due both to a direct toxic effect and a possible immune genetic susceptibility to SS. Also there are specific cytochrome P450 (CYP2) alleles that increase susceptibility to scleroderma in individuals who have been exposed to organic solvents. A study suggests that exposure to organic solvent may be a risk factor for developing systemic sclerosis [12]. We report a case of systemic sclerosis after exposure with toluene and benzene.

CASE REPORT

A 56-year old man who had worked in the tire factory for 20 years (8 years in vulcanization process and 12 years in extruding process) developed systemic sclerosis with skin and renal involvement after prolonged exposure to toluene and benzene by inhalation. About 11 years ago he developed coldness, stiffness, numbness, burning pain and discoloration of the fingers of hand, and to a lesser extent the feet on exposure to cold (Raynaud's phenomenon). Also he complained of impotency. He was admitted to the hospital because of the gangrene of first phalanges of right hand in January 2001. The patient had no history of dysphasia, fever or muscle weakness. He had asthma from childhood. He had quitted smoking 14 years ago. There was no familial history of collagen vascular disease. The patient took only bronchodilators for asthma and nifedipine for Raynaud's phenomenon through these years.

Physical examination showed blood pressure of 130/75 mmHg, a regular heart rate of 82/min, and a temperature of 36.5°. Skin examination revealed sclerodermatous skin changes of hands forearm and face, as well as sclerodactyly involving the hands, also restricted mouth opening; Telangectasia of face and trunk and digital ulceration of first finger of right hand was observed. There was generalized wheeze on lung examination. Cardiac and abdominal examination was normal. Lab tests showed (within normal range) for CBC,LFT, urine analysis, EKG,CXR ,RA factor, cold agglutinin, ANCA, ds-DNA C3,C4,CH50 were normal. HBs-Ag and HCV Ab was negative. Erythrocyte sedimentation rate (ESR) was 46mm/hr and a positive reaction for anti-nuclear antibodies (ANA) =5.6 (positive >1), Anti Centromer Ab and Anti SCL-70 Ab were negative. Respiratory function test showed moderate obstruction (FEV1=58%, FVC=68%, FEV1/FVC=64%).

Echocardiography was normal with ejection Fraction=45%.Coronary angiography showed ischemic heart disease. Angiography of both hands showed reduced diameter of palmar digit. He was considered to have limited type of systemic sclerosis. Forty days after the first admission he was admitted with complains of headaches, nausea, vomiting and detoriation of vision. Physical examination showed blood pressure of 180/100mmHg with a heart rate of 92/min. Lab test showed thrombocytopenia (PLT=27000) and rise of creatinine (1.7 mg/dl). Urine analysis detected mild proteinuria without any casts. Peripheral blood smear showed acantosis, helmet cell, and macrocytosis. The diagnosis of scleroderma renal crisis was made for patient. Renal dysfunction improved rapidly with ACE inhibitor. The diagnosis of diffuse systemic sclerosis was established for this patient through clinical and laboratory work up. After treatment with nifedipine (30 mg/day), prednisolone, methotrxate and removal from exposure a gradual resolution of the sclerodermatous lesion and skin tightening happened.

DISCUSSION

Systemic sclerosis is a multi factorial disease. Chlorine solvents, welding vapors, crystalline silica and various other solvents are environmental factors that increase the risk of systemic sclerosis [2].There are several reports that list the systemic sclerosis that caused by exposure to volatile organic solvents, in different places such as the below study. A study showed that 13 out of 28 men with SSc reported prior exposure to organic solvents [13]. There was a case report of SSc after 23 years of employment in a tire factory where there was potential for exposure to toluene, heptane, imethylbutylphenyldiamine, and octaphenol formaldehyde [14]. Of patients with systemic sclerosis in an eastern European series, 28% had suffered significant exposure to organic solvents [15]. Similarly, an Italian study has confirmed an etiological role of exposure to solvents in scleroderma [16]. In a Japanese series, generalized morphoeic lesions, similar to those found in occupational scleroderma, were found in nine of 115 patients with systemic sclerosis. Seven had been exposed to organic solvents before the onset of Raynaud's phenomenon. Some had visceral changes of systemic sclerosis [17]. A sclerodermatous syndrome consisting of cold sensitivity, restrictive lung defect, peripheral neuropathy, oesophageal dysfunction, labile hypertension and monoclonal paraproteinaemia has been reported in a man who had worked with many solvents. These included benzene, toluene, toluidine, xylene, xylidene, aniline compounds, and ethanolamine and its derivatives [18]. Exposure to solvents may be a provoking factor in female scleroderma but it does not seem to be a provoking factor for other connective tissue diseases [19].

Volatile organic compounds (aliphatic and aromatic hydrocarbon) that have been mainly used as a solvent in various industrial process [20].Tire building has some process such as mixing, blendering, calendaring, extruding and vulcanization. Solvents such as benzene and toluene produced during these procedures especially vulcanization .Our patient had worked in a no ventilated workplace, also the exposure level of benzene and toluene were more than threshold exposure limit. Almost all patients with systemic sclerosis manifest Raynaud's phenomenon [4]. He mentioned the same symptoms (Raynaud's phenomenon) in one of his coworkers that quitted his work. Nevertheless, early diagnosis should be done in an industry which there is potential risk of exposure to

solvents. Raynaud's phenomenon is the first symptom in up to 70% of patients with SSc.

We suggest that a review of solvent exposure should include in the annual checkup of workers from relevant industries. In patients in whom Raynaud's phenomenon is present a complete physical examination, and if necessary lab test such as anti-nuclear antibodies (ANA) should be carried out, and further exposure avoided.

As a consequence these solvents have a many negative health effect on the workers. To prevent health effects on the use of personal protective equipment, occupational health , air conditioning and health education for workers is necessary.

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