Systemic Sclerosis Associated with Occupational Exposure to Solvents

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1. Abstract

1.1. Background: Systemic Sclerosis (SS) is a rare multisystemic disorder with changes in the immune system, vascular and connective tissue. Furthermore, there is an increase in the synthesis and accumulation of collagen and extracellular matrix components in the skin and internal organs, with repercussions on the lungs, gastrointestinal tract, heart and kidneys. SS occurs in susceptible individuals and is triggered by poorly understood factors. There is evidence of genetic susceptibility, however studies show under 5% of agreement between monozygotic twins, pointing that environmental factors play a role in this immunological dysregulation. Since 1950 there have been reports of occupational risk factors in SS development, such as infectious agents, neoplasms, exposure to vinyl, silica, metals and solvents.

1.2. Methods: We report a case of a young man who developed SS after working for more than 15 years exposed to various solvents.

1.3. Results: The mechanism by which solvents act in the pathogenesis of SS remains unclear.

1.4. Conclusions: It is likely that many occupational SS have not had the causal relationship recognized, thus, probably a review of the occupational exposures would lead to a greater identification of the environmental relation to SS, with a better knowledge of the toxic agents involved in its onset leading to the exclusion of these substances from the professional environment.

3. Introduction

Systemic Sclerosis (SS) is a rare multisystemic disorder with changes in the immune system, vascular and connective tissue. There is presence of autoantibodies, CD4 + perivascular inflammatory infiltrate, increased expression of adhesion molecules in vessels and interstitium; alteration of microvasculature with endothelial damage, reduction of capillaries and arterial thickening, producing an obstructive vasculopathy. Furthermore, there is an increase in the synthesis and accumulation of collagen and extracellular matrix components in the skin and internal organs, with repercussions on the lungs, gastrointestinal tract, heart and kidneys [1, 2]. The progression of the disease is variable requiring sequential and simultaneous dysfunction of various regulatory mechanisms.

The incidence of SS is 4.5 to 18.7 new cases per million inhabitants in Europe and the United States [3].

Since 1950 there have been reports of occupational risk factors in SS development [1]. Epidemiological evidence of several environmental risk factors has already been analyzed [1], such as infectious agents, neoplasms, exposure to vinyl, silica, metals and solvents [4].

These exposures are often of long duration and the degree of exposure is related to a greater risk of developing the disease [1]. The most recognized occupational exposure associated to SS is solvents [2].

There is no pathognomonic test for SS and the idiopathic and occupational diseases are indistinguishable clinically, serologically and immunologically [5].

Discontinuation of exposure to the agent may stabilize the disease progression and lead to an improvement in the clinical picture 5.
There is no drug that changes the natural course of the disease, but there are several possibilities of treatment depending on the organ involved [6].

Despite the several articles published relating occupational exposure to solvents to SS, there is still great ignorance of this relationship by physicians who treat patients and by those responsible for the characterization of the causal nexus. This implies in a delay in the diagnosis, treatment, and especially in the necessary changes of the work environment, with medical-legal and social security consequences.

SS classically occurs more in women aged 30 to 50 years, with an incidence reported up to 14 times higher than in men [7]. On the other hand, when we consider SS caused by solvents, the risk is higher in men and does not depend on the dose of exposure [2]. We report a case of a young man who developed SS after working for more than 15 years exposed to various solvents.

4. Patients and Methods

DMS, 38 years old, male, white, assembler in a mechanical workshop for 17 years. His main activities were paintings and general mechanics, with daily exposure to oil, inks, glues, gasoline, kerosene, thinner and others solvents. He received individual protective equipment, such as hand cream, rubber boots, shirt, pants, leather shoe, protector headset, cotton jacket, nitrile glove and leather glove. He used to work in a shed, windowless, with poor ventilation.

About 7 years ago he started to present reddish spots on the skin of his arms, legs and trunk, associated with difficulty swallowing and dizziness. He performed a skin biopsy, diagnosed with scleroderma. Two years later, he started with joint pain, what led to the use of methotrexate (MTX), 10 mg per week.

Five years later, he started to present high blood pressure and was diagnosed with hypertension. Currently he uses MTX 15mg per week, lanzoprazol, zolpiden, cloxazolan, clobazan and maxopran. He has difficulty to swallow, heartburn and an important gastro-esophageal reflux that forces him to sleep with several pillows. He maintains joint and cervical pains despite the treatment.

5. Physical Exam

Good general condition. Eupneic. Rare brownish macules isolated in the trunk, upper and lower limbs, with slight atrophy (Figure 1). Hands with slight thickening of skin digits (Figure 2). Eurostar-01 Scale Score.

6. List of Tests


Esophageal scintigraphy 10/2016 - Normal.


Laboratory 08/2017- Anti DNA- Native 1:10; VHS 3.

7. Discussion

Autoimmune diseases include dozens of different diseases characterized by pathological auto reactive immune responses and high associated morbidity and mortality [1, 8].

SS occurs in susceptible individuals and is triggered by poorly un-
nderstood factors [9]. Prevalence ranges from 50 to 300 per million depending on the population studied [7]. Patients with systemic disease present great clinical variation, although almost all have Raynaud’s phenomenon (RP) and esophageal dysmotility, up to 80% present pulmonary arterial hypertension; cardiac impairment; interstitial lung disease; inflammatory arthritis and digital ulcers [1, 6].

A variety of studies have shown evidence of the genetic contribution to the susceptibility and expression of the disease. The risk in first-degree relatives with SS showed to be increased. However, since studies show under 5% of agreement between monozygotic twins, the mechanism by which these autoantigens are triggered suggests that environmental factors play a role in this immunological dysregulation 3;10 and may include, among other things, eating habits, exposure to chemical agents, hygiene conditions, smoking and sun exposure [1, 11].

If such exogenous elements are present at the work environment, such as exposure to certain chemical and infectious agents, the disease, even if autoimmune, should be named as an occupational disease, as in Systemic Sclerosis associated with exposure to silica, also called the Erasmus Syndrome [12].

A number of environmental agents have been implicated in SS development as seen in Table 1 [6, 13, 14, 15 - 17]. Not all causal elements are solvents properly, some share structural similarities such as vinyl chloride, and others contain solvents in the formulation, such as epoxy resins [1].

Group of Marie et al. found also a significant association between some metals (antimony and platinum in men and antimony, cadmium, lead, mercury, palladium and zinc in women) with SS [4]. Some drugs have been associated with the development of SS like syndromes, like bleomycin, pentazocine, cocaine and taxanes (docetaxel, paclitaxel) [18].

Table 1- Environmental agents implicated in SS development [1, 4, 6, 13, 14, 15, 16, 17, 18].

When these exogenous factors are derived from an exposure in the workplace, the disease should be classified as occupational, as in the case presented here.

There is no specific laboratory test for the diagnosis of SS and there is no marker to differentiate occupational and idiopathic disease, although there are different clinical nuances, such as a higher prevalence and severity of lung disease in silica exposure [5] and a greater severity of occupational SS; in addition to the latter being more frequent in men [2, 19]. Occupational exposure to organic solvents is therefore a predictor of SS severity [2].

The mechanism by which solvents act in the pathogenesis of SS remains unclear [2]. They are widely used in various activities such as dry cleaning (tetrachlorethylene), painting (thinner, toluene), enamel removers and glue solvents (acetone, methyl acetate, ethyl acetate), stain removers (hexane) [2], being present in countless professions, such as manufacturing and repairing of vehicles engines, ships, aircraft; tire production, plastics, varnishes, paints, enamels, cements, adhesives, oils, footwear, animal and synthetic leather goods, metals; in the paper and dye industry, printing works, laundries, among others [2]. Our patient reported continuous and chronic occupational exposure to various types of solvents, paints and chemical diluents for about 17 years, which is compatible with the profession of vehicle mechanic. However, even with the diagnosis of the disease a few years ago, he had never been told to avoid contacts or change profession. Interestingly, the fact that the disease is autoimmune seems to induce doctors to ignore their relation to work.

To date, research on the role of plasticizers, phthalates, bisphenol A; organochlorine pesticides, polychlorinated biphenyls, dioxins and furanspecific agents; organic halogened pollutants derived from motor vehicles; breast implants, hair dye, prosthetics and contact lenses; asbestos; exposure to ionizing radiation, ultraviolet radiation and electric and magnetic fields; infections, diets, foods and dietary contaminants did not show a convincing greater risk for SS development [2].

Similarly, breastfeeding, age of food introduction; early exposure to complex foods; low intake of antioxidants, fruits or fibers and high intake of sweets or fat; low alcohol consumption; and the consumption of food chemicals, such as dyes or additives, nitrates, nitrates and nitrosamines showed no relation to the development of SS 2. Although smoking does not pose a major risk to the onset of SS, smokers present significant vascular and pulmonary SS disease [2].

The repercussions of SS on personal and work life are huge. A recent French study showed that the disease generates loss of employment (41%) and a decrease in income (31%), generally secondary to asthenia, RP, arthralgias and digital ulcerations [20].

SS treatment may be disappointing, penicillamine has been used for skin lesions, calcium channel blockers may help in the RP, as well as, sildenafil and similar 6. Our patient was undergoing rheumatologic follow-up for several years, using methotrexate, with partial control of the condition, but without leaving the activity until less than 1 year before our evaluation.
Considering that there is no positive family history for rheumatological and dermatological diseases, the work since youth at automobile mechanics, being exposed daily and chronically to solvents, without adequate protection, allowed us to consider that the occupational exposure in this case was the exogenous factor triggering SS.

Even with the relation between SS and solvents identified more than 50 years ago, there still remains a lack of knowledge by the doctors who first receive these patients, either the occupational physician, rheumatologist, dermatologist, or the social security medical expert responsible for determining the causal link between work and disease. It is likely that many occupational SS have not had the causal relationship recognized, thus, probably a review of the occupational exposures would lead to a greater identification of the environmental relation to SS diagnosis, with a better knowledge of the toxic agents involved in its onset and the exclusion of these substances from the professional environment.

The patient is away from the activity and was advised to a change of job, in line with the thinking of other authors [9].

8. Conclusions
Exposure to solvents is clearly and strongly associated with SS development and should be recognized as an occupational disease when it occurs at the workplace.

Considering the long exposure of our patient to agents involved in the onset of SS, we discuss the need to investigate exposure to occupational agents in this disease in order to prevent the occurrence of more severe forms of the disease, as well as to implement changes in the work environment.

References


