AnnalsofClinicalandMedicalCaseReports

CaseReports

SystemicSclerosisAssociatedwithOccupationalExposure to Solvents

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2. Key words

Scleroderma- Solvents- Sclero-derma; Systemic- Occupational Disease

1. Abstract

Background: SystemicSclerosis(SS)isararemultisystemicdisorderwithchangesintheimmunesystem, vascular and connective tissue. Furthermore, there is an increase in the synthesis and accumulation of collagen andextracellularmatrixcomponentsintheskinandinternalorgans,withrepercussionsonthelungs,gastrointes-tinaltract,heartandkidneys.SSoccursinsusceptibleindividualsandistriggeredbypoorlyunderstoodfactors. Thereisevidenceofgeneticsusceptibility,howeverstudiesshowunder5%ofagreementbetweenmonozygotic twins,pointingthatenvironmentalfactorsplayaroleinthisimmunologicaldysregulation.Since1950therehave been reports of occupational risk factors in SS development, such as infectious agents, neoplasms, exposure to vinyl, silica, metals and solvents.

Methods: WereportacaseofayoungmanwhodevelopedSSafterworkingformorethan15yearsexposed to various solvents.

Results: ThemechanismbywhichsolventsactinthepathogenesisofSSremains unclear.

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 relationtoSS,withabetterknowledgeofthetoxicagentsinvolvedinitsonsetleadingtotheexclusionofthese 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+perivascularinflammatoryinfiltrate,increasedex- pression 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 re- percussions on the lungs, gastrointestinal tract, heart and kidneys [1, 2]. Theprogressionofthediseaseisvariablerequiringsequentialandsimul - taneous 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 de- velopment [1]. Epidemiological evidence of several environmental risk factors has already been analyzed [1], such as infectious agents, neo- plasms, exposure to vinyl, silica, metals and solvents [4].

Theseexposuresareoftenoflongdurationandthedegreeofexposureis

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relatedtoagreaterriskofdevelopingthedisease[1].Themostrecognized occupational exposure associated to SS is solvents [2].

ThereisnopathognomonictestforSSandtheidiopathicandoccupational diseases are indistinguishable clinically, serologically and immunologi- cally [5].

Discontinuation of exposure to the agent may stabilize the disease pro- gressionandleadtoanimprovementintheclinicalpicture5.Thereisno drug that changes the natural course of the disease, but there are several possibilities of treatment depending on the organ involved [6].

Despitetheseveralarticlespublishedrelatingoccupationalexposure to solvents to SS, there is still great ignorance of this relationship by physicians who treat patients and by those responsible for the characterizationofthecausalnexus.Thisimpliesinadelayinthe diagnosis,treatment,andespeciallyinthenecessarychangesofthe work environment, with medical-legal and social security conse- quences.

SSclassicallyoccursmoreinwomenaged30to50years,withan incidencereportedupto14timeshigherthaninmen[7].Ontheother

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hand, when we consider SS caused by solvents, the risk is higher in men anddoesnotdependonthedoseofexposure[2].Wereportacaseof a young man who developed SS after working for more than 15 years exposed to various solvents.

4. PatientsandMethods

DMS, 38 years old, male, white, assembler in a mechanical workshopfor 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,legsandtrunk,associatedwithdifficultyswallowinganddizziness. Heperformedaskinbiopsy,diagnosedwithscleroderma.Twoyearslater, hestartedwithjointpain,whatledtotheuseofmethotrexate(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 ofTests

Histopathology 10/2011- Lumbar skin- compatible with scleroderma.

Esophagealmanometry12/2011-Loweresophagealsphincterhypotonia.

Chest Tomography 11/2013- Normal.

Esophagealmanometry11/2013-Ineffective,moderateesophageal motility.

Laboratory 10/2014- Anti DNA: Native negative. Lupus anticoagulant: positive.

Esophageal scintigraphy 10/2016 - Normal.

Echocardiography10/2016-Normal.Spirometry11/2016-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].

SSoccursinsusceptibleindividualsandistriggeredbypoorlyunderstood factors[9].Prevalencerangesfrom50to300permilliondependingon

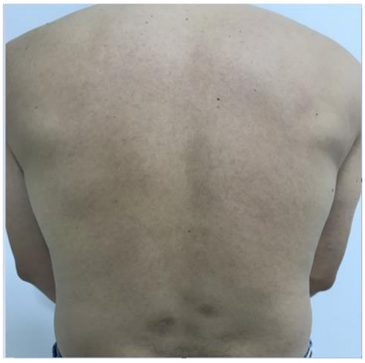

Figure 1: Good general condition. Eupneic. Rare brownish macules iso- lated in the trunk, upper and lower limbs, with slight atrophy.

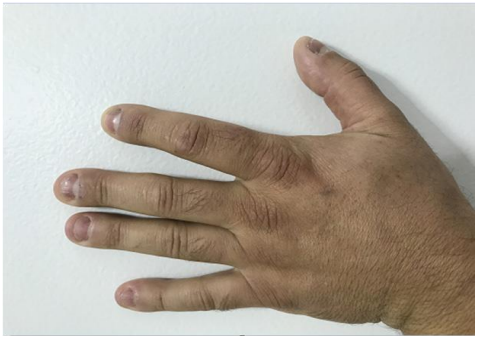

Figure 2: Hands with slight thickening of skin digits . Eurostar-01 Scale Score.

the population studied [7]. Patients with systemic disease present great clinicalvariation,althoughalmostallhaveRaynaud'sphenomenon (RP) and esophageal dysmotility, up to 80% present pulmonary arterial hypertension;cardiacimpairment;interstitiallungdisease;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 whichtheseautoantigensaretriggeredsuggeststhatenvironmentalfactors 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].

Ifsuchexogenouselementsarepresentattheworkenvironment,suchas exposure to certain chemical and infectious agents, the disease, even if autoimmune,shouldbenamedasanoccupationaldisease,asinSystemic Sclerosis associated with exposure to silica, also called the Erasmus Syndrome [12].

Anumberof environmental agents have been implicated in SS development asseeninTable1[6,13,14,15-17].Notallcausalelementsaresolvents properly, some share structural similarities such as vinyl chloride, and others contain solvents in the formulation, such as epoxy resins [1].

GroupofMarieetal.foundalsoasignificantassociationbetween some metals (antimony and platinum in men and antimony, cadmium, lead, mercury, palladium and zinc in women) with SS [4]. Some drugs havebeenassociatedwiththedevelopmentofSSlikesyndromes,like

bleomycin,pentazocine,cocaineandtaxanes(docetaxel,paclitaxel)[18].

Table1-EnvironmentalagentsimplicatedinSSdevelopment[1,4,6,13, 14, 15, 16, 17, 18].

When these exogenous factors are derived from an exposure in the workplace,thediseaseshouldbeclassifiedasoccupational,asinthecase presented here.

There is no specific laboratory test for the diagnosis of SS and there isno 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].Occupationalexposuretoorganicsolventsisthereforeapredictorof SS severity [2].

The mechanism by which solvents act in the pathogenesis of SS remains unclear[2].Theyarewidelyusedinvariousactivitiessuchasdrycleaning (tetrachlorethylene), painting (thinners, toluene), enamel removers and glue solvents (acetone, methyl acetate, ethyl acetate), stain removers (hexane)[2],beingpresentincountlessprofessions,suchasmanufacturing andrepairingofvehiclesengines,ships,aircraft;tireproduction,plastics, varnishes,paints,enamels,cements,adhesives,oils,footwear,animaland synthetic leather goods, metals; in the paper and dye industry, printing works,laundries,amongothers[2].Ourpatientreportedcontinuous 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 ofthe 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 halogenated pollutants derived from motor vehicles; breast implants, hair dye, prosthetics and contact lenses; asbestos;exposuretoionizingradiation,ultravioletradiationandelectric andmagneticfields;infections,diets,foodsanddietarycontaminantsdid not show a convincing greater risk for SS development [2].

Similarly, breastfeeding, age of food introduction; early exposure to complexfoods;lowintakeofantioxidants,fruitsorfibersandhighintake of sweets or fat; low alcohol consumption; and the consumption of food chemicals, such as dyes or additives, nitrates, nitrites 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 Frenchstudyshowedthatthediseasegenerateslossofemployment(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,calciumchannelblockersmayhelpintheRP,aswellas,sildenafil andsimilar6.Ourpatientwasundergoingrheumatologicfollow-upfor severalyears,usingmethotrexate,withpartialcontrolofthecondition,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 adequateprotection,allowedustoconsiderthattheoccupationalexposure in this case was the exogenous factor triggering SS.

Even with the relation between SS and solvents identified more than 50 yearsago,therestillremainsalackofknowledgebythedoctorswhofirst 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 greateridentificationoftheenvironmentalrelationtoSSdiagnosis,witha betterknowledgeofthetoxicagentsinvolvedinitsonsetandtheexclusion of these substances from the professional environment.

Thepatientisawayfromtheactivityandwasadvisedtoachangeofjob, in line with the thinking of other authors [9].

8. Conclusions

Exposure to solvents is clearly and strongly associated with SS developmentandshouldberecognizedasanoccupationaldiseasewhenit occurs at the workplace.

Consideringthelongexposureofourpatienttoagentsinvolvedintheonset ofSS,wediscusstheneedtoinvestigateexposuretooccupationalagents inthisdiseaseinordertopreventtheoccurrenceofmoresevereformsof the disease, as well as to implement changes in the work environment.

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