

Mycosis fungoides Progression and Chronic Solvent Exposure

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Key Words

Solvent · Mycosis fungoides · Occupational exposure · T-cell receptor rearrangement · Interferon- α

Abstract

The effect of repeated exposure to specific chemicals on the initiation or progression of mycosis fungoides (MF) remains unsettled. A patient with low-grade patch stage MF progressively developed MF plaques restricted to his arms, and a tumour on his right thigh. These areas were subject to repeated exposure to solvents. His thigh was indeed in close contact with his trousers pocket where he used to store a wiping rag drenched into white spirit and cellulosic thinner. Immunophenotyping these lesions revealed a dense LCA+, CD2+, CD3+, CD4+, CD5+, CD7+, CD45+, CD45RO+ T-cell infiltrate admixed with many factor XIIIa+ dendrocytes. T-cell receptor rearrangement analysis identified a monoclonal T-cell infiltrate. An internal work-up remained negative. Stopping further solvent exposure failed to improve his condition. Oral corticotherapy combined with low-dose interferon- α 2a halted disease progression. This observation suggests that long-term solvent exposure may trigger MF and hasten its progression from the patch stage to the plaque and tumour stages.

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Case Report

A 52-year-old man, who has been a professional painter since the age of 16, suffered from hypertension and insulin-dependent diabetes. He was treated by metformine (Glucophage[®]), human insulin (Actrapid[®] and Insulatard[®]), and captopril (Capoten[®]). He presented with a 2-year history of patch stage mycosis fungoides (MF) predominantly involving his arms and to a lesser extent his back and thorax. The diagnosis of MF was confirmed by histology and immunohistology showing a moderately dense lymphoid cell infiltrate composed of CD45+, LCA+, CD45RO+, CD2+, CD3+, CD4+, CD5+, CD7+ T-cells admixed with numerous factor XIIIa+ dendrocytes. The immunoreactivity for CD1a, CD45RA, CD20, CD30, CD56, CD79a, C3, IgM, IgA, IgG, and the κ - and λ -light chains was not contributive. T-cell receptor and immunoglobulin rearrangements were not detected. Standard patch tests and prick tests searching for allergy remained negative. The haemogram and physical examination were unremarkable. Potent topical corticosteroids improved the clinical severity although MF patches recurred occasionally.

One year later, the patient developed a circinate tumour confined to his right thigh (fig. 1). Histology and immunophenotyping were consistent with the tumoral stage of MF (fig. 2). A monoclonal T-cell receptor γ gene population was disclosed by polymerase

chain reaction amplification. IgH loci VNDNJ rearrangement was absent.

Physical examination was otherwise unremarkable without any detectable lymphadenopathies. Further internal workup, including a chest X-ray and scans of the chest, abdomen and pelvis were normal. Peripheral blood cell counts and organ chemistry were in the normal ranges. In particular, Sézary cells were not detected in the peripheral blood. Bone marrow biopsy was unremarkable. The internal work-up was repeated 6 and 12 months later and revealed no evidence for extracutaneous involvement.

In his professional life, the patient used to clean his arms with solvents several times a day, resulting in repeated exposure for about 35 years. Furthermore, he used to clean paint drops with a piece of rag drenched into the same solvents. He stored this wiping rag in the right pocket of his trousers, entertaining a continuous solvent exposure restricted to a focal area of his right thigh. White spirit and cellulosic thinner were the solvents used by the patient since his earliest professional life.

The MF tumour of our patient failed to regress spontaneously after stopping the chemical exposure. Stage-adapted therapy was initiated following current recommendations [1]. Once weekly intralesional triamcinolone acetonide injections (Albicort[®], 40 mg/ml) were followed by a progressive regression of the lesion. However, due to over-

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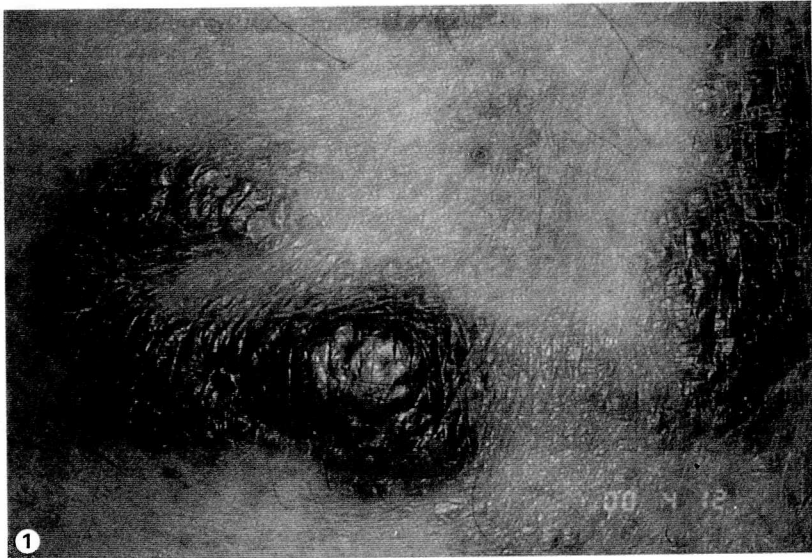


Fig. 1. Tumoral MF restricted to the thigh.

all disease progression, oral methylprednisolone (Medrol®, 64 mg daily, followed by progressive tapering) was administered. An initially favourable response was obtained. However, his diabetes became unstable. Hence, a combination treatment was initiated. Methylprednisolone (8 mg o.d.) and $10 \cdot 10^6$ IU subcutaneous injections of interferon- $\alpha 2a$ three times weekly led to clinical regression after 5 weeks. The biological and clinical tolerances remained acceptable and the disease was kept in remission for the next 18-month follow-up.

Comments

We present the case of a professional painter with patch stage MF who developed progressively infiltrated plaques on his arms and a tumour on his right thigh. These two more severe clinical grades of MF matched with two increasing levels of occupational solvent exposure. First, the repeated contact exposure to the solvents on his forearms during skin cleansing corresponded to the site where patch stage MF progressed to plaques. Second, the more severe and sustained solvent exposure of the thigh corresponded to the location of the single MF tumour. Hence, this case suggests a possible link between chronic occupational exposure to solvents and MF progression.

What Is the Evidence for Chemically-Induced or Boosted MF?

At the interface with the environment, the skin is in contact with many xenobiotics. Cutaneous consequences of local toxic effects is probably far more prevalent than is generally recognized [2]. The increasing MF incidence may suggest that environmental threats may play a pathogenic role [3–5]. However, the relationship between chronic occupational exposures to chemicals and MF remains unclear [3–9]. A history of multiple exposure to noxious chemicals was previously reported in 91% of MF patients [7]. In this survey, the mean duration of exposure to chemicals averaged 13 years. The most common xenobiotics were air pollutants (39%), pesticides (36%), solvents (30%), detergents and disinfectants (14%). The influence of occupational exposure was also suggested by the higher MF mortality rate in industrial areas involved in the petroleum, rubber, primary and fabricated metal, machinery, and printing activities [10]. A



Fig. 2. CD2+ T-cells in MF tumour of the thigh.

case-control study of 59 cutaneous T-cell lymphoma patients indicated a 4.3 relative risk for patients in the manufacturing and construction industries [11].

Some studies did not confirm the association between occupational exposure to chemicals and MF [6–8]. However, chronic inflammatory skin diseases, in particular allergic dermatoses, were considered as a risk factor for developing MF [7, 8]. An epidemiological study including 174 cutaneous T-cell lymphoma patients and 294 controls did not reveal a positive correlation between long-term exposure to chemicals and cutaneous T-cell lymphoma [11].

MF is the most frequent peripheral non-Hodgkin T-cell lymphoma [12]. Its initial presentation is on the skin and exhibits distinct clinical, histological, phenotypic and genotypic features [12, 13]. The disease usually progresses through patch, plaque and tumour stages before lymph nodes and internal organs may become involved. MF is composed of neoplastic Th2 cells admixed with other non-malignant Th1 cells, and

CD1a+, CD36+ and factor XIIIa+ dendritic cells [14]. MF progression and regression are balanced by complex interactions between the malignant T cells, the reactive non-malignant T cells and the activated dendritic cells.

The presently reported patient suffered from low-grade patch stage MF. This professional painter developed MF plaques on his arms which he repeatedly cleaned with solvents. Furthermore, he developed an MF tumour restricted to his right thigh at a site subject to sustained exposure to cellulosic thinner and white spirit. White spirit (CAS No. 64742-82-1) is an inflammable aromatic hydrocarbonated solvent containing 16% aromates and less than 1% benzene, toluene and xylene. The safety data sheet mentions

the risk of skin dryness without allergic sensitisation following contact. Toxicological data report LD (lethal dose) 50 in rats over 5 g/kg when administered orally and 3.4–5.5 mg/m³ (4 h) by inhalation. There are no animal and human data on the long-term exposure effects and on the carcinogenicity of this solvent. Cellulosic thinner is a mixture of toluene (CAS No. 108-88-3), butanone (CAS No. 78-93-3), and butanol (CAS No. 78-83-1). Toxicological and carcinogenicity data are not available for these substances. It is an inflammable solvent, irritant for the skin and the upper airways. Xerosis is observed after repeated applications. No contact sensitisation has been reported so far.

In our patient, in addition to the long-term exposure to the solvents, the long-term

use of paints could also be suspected to cause MF. However, the wide variety of paints and the changes in time in their components did not lead to long-term exposures to specific agents as experienced with the solvents.

Conclusion

This case suggests that prolonged exposure to solvents might trigger MF progression from patch to plaque and tumour stages. This observation calls for a better definition of the role of chronic exposure to solvents and other noxious xenobiotics in MF.

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