

Internal Dissemination of Mycosis fungoides despite Successful Local Therapy

Torkel Fischer,¹ Willem A. van Vloten² and Gunnar Volden³

¹Department of Dermatology, University Hospital, Uppsala, Sweden, ²Department of Dermatology, University Hospital, Leiden, The Netherlands, and ³Department of Dermatology, Rigshospitalet, Oslo, Norway

Received July 11, 1977

Key words: Electron irradiation; Mycosis fungoides; Nitrogen mustard; Photochemotherapy; Trioxalen

Prediction of the course of mycosis fungoides is still impossible, despite thorough examination and staging of the disease before treatment. Since several forms of potent local treatment are now available for this disease, such as topical nitrogen mustard (11), total skin electron irradiation (3), and psoralen combined with long wave ultraviolet light (2, 4), we must watch for signs of internal dissemination of the disease even when the skin is free from mycosis fungoides lesions. This is illustrated by the case histories of three patients initially considered to be free from lymph node or internal dissemination after successful local treatment but who subsequently developed disseminated lymphoma without any skin lesions.

Patient 1

A healthy 45-year-old man suffered from slowly spreading skin lesions on the trunk and extremities for a year before coming to the Department of Dermatology of the Leiden University Hospital. The skin lesions consisted of infiltrated annular plaques which were partially crusted and exudative. The clinical diagnosis mycosis fungoides was confirmed histologically and cytophotometrically (7). Staging investigations, including lymphangiography, liver and spleen scintigraphy, and blood morphology and biochemistry, revealed no abnormalities. Histological investigation of a lymph node showed only some fibrosis and hyperplasia; no signs of dissemination were present.

On the basis of the results of all investigations the dis-

case was regarded as purely cutaneous and the patient was treated with total skin electron irradiation up to 3800 rad, 4 MeV (8). A resistant tumour behind the left ear was additionally X-irradiated. At the end of the treatment some erythematous lesions persisted and the skin was subsequently treated with topical nitrogen mustard (11). All skin lesions disappeared completely. Two months later the patient's general health deteriorated and he complained of pain on the left side of his back. A lymph node in the axilla became enlarged. Five weeks later paresis of the legs developed. Myelography showed a complete block at the level of Th 3, which surgical exploration showed to be due to an extradural tumour. Histologically this tumour was interpreted as lymphoma.

Treatment was started with local X-irradiation of the tumour, but the patient's condition continued to deteriorate rapidly and he died in a uraemic and comatous state 2 years after the appearance of the first skin lesions. The autopsy showed that the malignant lymphoma had infiltrated the retroperitoneal tissue, all of the lymph nodes and the head of the pancreas; the skin was completely normal, however. Histological investigation revealed variably large mononuclear cells with large nuclei, prominent nucleoli and abundant cytoplasm. There was a high mitotic activity. The tumour was classified as lymphoblastic lymphoma.

Patient 2

A 71-year-old man suffered from mycosis fungoides for 20 years and skin tumours for 10 years. Earlier treatment had included P₃₂, topical nitrogen mustard, additional Röntgen therapy, and Bleomycin® systemically. None of these treatments healed his skin permanently, and about 30% of the skin surface was affected with erythema, infiltration, and multiple tumours 2–5 cm in size. Careful staging according to the Scandinavian Mycosis Fungoides Study Group (6), including blood morphology and chemistry, chest and skeletal X-rays, lower limb lymphangiography, and cytology of an enlarged inguinal lymph node, disclosed no signs of internal dissemination. On the basis of these results we started local treatment with trioxalen baths combined with UV light from a dysprosium solarium (1). Intense treatment for 6 months completely healed his skin, both clinically and histologically. Small scars showed where the tumours had been located. Maintenance treatment kept him nearly free of lymphoma. A few small new infiltrations disappeared with a higher maintenance dosage of UV light. His skin had been healed for almost 6 months when his red blood cell count suddenly dropped critically and he developed a severe pancytopenia. Sternal bone marrow samples showed arrest of the ripening of the red blood cells but even then we were unable to find signs of internal dissemination of the lymphoma. The patient was given blood transfusions, corticosteroids and androgens. None of these treatments stimulated his bone marrow, and when he died 3 months later from septicaemia his skin was still free of mycosis fungoides. The autopsy showed infiltration in the liver, spleen, and vertebrae with a microscopical picture of a polymorphic mixed histiocytic and lymphocytic type of malignant lymphoma.

Patient 3

In this 69-year-old previously healthy man the diagnosis mycosis fungoides had been made both clinically and histologically 11 years earlier. Despite intermittent treatment with Grenz-ray and Röntgen irradiation the lesions had increased. In April 1976, before topical treatment with nitrogen mustard was started, he displayed several heavily infiltrated plaques and some tumours, especially on the lower extremities. The usual work-up for malignant lymphoma revealed no abnormalities. He was treated with whole-body topical applications of aqueous solutions of nitrogen mustard and additionally hydration of tumours and plaques with the same solution (10). Complete remission of all skin lesions was achieved after 2½ months of treatment. Maintenance treatment once a week kept his skin in a disease-free condition. In March 1977, 9 months after complete remission of the skin lesions, he noticed enlarged inguinal lymph nodes. Lymphangiography showed pathologically enlarged lymph nodes in the left inguinal and iliacal region. Cytology of one of these confirmed the lymphoma diagnosis. No other sign of internal dissemination was found. Systemic chemotherapy was started, which resulted in a decrease of the enlarged lymph nodes.

DISCUSSION

Mycosis fungoides usually has a slowly progressing course. Internal dissemination occurs mainly in the advanced stages. Analysis of autopsies in mycosis fungoides reported in the literature showed involvement of internal organs up to 72% (5). To justify restriction of therapy to the skin, we must be certain that the disease has not spread to other organs. Therefore, careful staging procedures have been instituted in different countries. The investigations include histology of the skin and palpable lymph nodes, lymphangiography, scintigraphy of the liver and spleen, analysis of bone marrow aspirates, and blood chemistry. No good parameters are available for the exclusion of internal dissemination, especially in patients whose skin lesions are successfully treated, and the question of the extent to which staging procedures should be performed is still unanswered. In advanced stages, lymphopenia may be a valuable sign of dissemination. In patient 1 we only found a mild leukocytosis. Palpable lymphadenopathy is associated with a poor prognosis (3), which raises another question, viz., whether a dermatopathic lymph node should be regarded purely as a reactive lymph node. In patient 2 enlarged inguinal lymph nodes with a benign cytology were present for more than a year. Laparotomy combined with biopsies of the liver and lymph

nodes and splenectomy may give more prognostic information on mycosis fungoides (9). However, laparotomy has a certain risk for the patient, and this procedure is therefore still under discussion. Aggressive use of topical nitrogen mustard and electron-beam therapy is associated with long-term remissions in patients with mycosis fungoides (3, 11). Though satisfied by the cured skin, we may meanwhile be masking the signs of dissemination. The presented case histories underline the importance of the question whether mycosis fungoides starts in the skin, which might justify the treatment of the skin only, or whether it is a generalized lymphoma from the very outset, for which both topical treatment and internal cytostatic therapy are needed.

REFERENCES

1. Fischer, T. & Alsins, J.: Treatment of psoriasis with trioxalen baths and dysprosium lamps. *Acta Dermatovener (Stockholm)* 56: 383, 1976.
2. Fischer, T. & Skogh, M.: Malignant cutaneous reticulosis treated with trioxalen baths and dysprosium lamps. *Proc. of the XXI Nordisk Dermatologkongress Aarhus* 26-29 june, 1977.
3. Fuks, Z. A., Bagshaw, M. A. & Farber, E. M.: Prognostic signs and the management of the mycosis fungoides. *Cancer* 32: 1385, 1973.
4. Gilchrist, B. A., Parrish, J. A., Tanenbaum, L., Haynes, H. A., Fitzpatrick, T. B.: Oral methoxsalen photochemotherapy of mycosis fungoides. *Cancer* 38: 683, 1976.
5. Levi, J. A. & Wiernik, P. H.: Management of mycosis fungoides—Current status and future prospects. *Medicine* 54: 73, 1975.
6. Molin, L., Groth, O. & Thomsen, K.: Behandling av mycosis fungoides—ett internordiskt projekt. *Nordisk Medicin* 91: 121, 1976.
7. Van Vloten, W. A., van Duijn, P. & Schaberg, A.: Cytodiagnostic use of Feulgen-DNA measurements in cell imprints from the skin of patients with mycosis fungoides. *Br J Dermatol* 91: 363, 1974.
8. Van Vloten, W. A., Vermey, J. & de Vroome, H.: Total skin electron irradiation in mycosis fungoides. *Dermatologica* 155: 28, 1977.
9. Variakojis, D., Rosas-Urbe, A. & Rappaport, H.: Mycosis fungoides—Pathological findings in staging laparotomies. *Cancer* 33: 1589, 1974.
10. Volden, G. & Larsen, T. E.: Remissions of mycosis fungoides induced by nitrogen mustard (HN2). *Dermatologica*, in press.
11. Vonderheid, E. C., van Scott, E. J., Johnson, W. C., Grekin, D. A. & Asbell, S. O.: Topical chemotherapy and immunotherapy of mycosis fungoides. *Arch Dermatol* 113: 454, 1977.