Scabies Associated with Radiation Therapy for Cutaneous T-Cell Lymphoma

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Abstract. Scabies, infection with Sarcoptes scabiei, is known to be predisposed to by poor body hygiene, environmental exposure, and systemic immunodeficiency. We report the case of an 83-year-old man with Sezary’s syndrome who developed scabies limited to the skin of the upper chest, the same location where he had previously received electron beam radiation treatments for cutaneous T-cell lymphoma. Histologic and immunohistochemical studies demonstrated that sections of the previously irradiated right and left chest skin, compared to non-irradiated chest, abdominal, and leg skin, had infestation by scabies, diminished involvement by T-cell lymphoma, and notably reduced numbers of Langerhans cells. These findings suggest that the development of scabies may be predisposed to by local cutaneous radiation therapy, and that it may be mediated by local cutaneous immunodeficiency secondary to reduced numbers of Langerhans cells. (received 8 June 2000; accepted 15 September 2000)

Keywords: Scabies, radiation, Langerhans cells, immunodeficiency, cutaneous T-cell lymphoma.

Introduction

Scabies, infestation with the human itch mite Sarcoptes scabiei var. hominis, is transmitted by direct human (or occasionally non-human) contact. Overviews of this organism and its epidemiology, clinical manifestations, pathology, pathogenesis/etiology, and diagnosis have recently been published [1,2]. Scabietic nodules may result from persisting antigens of mite parts and an immune response may help to limit the number of infesting organisms, either directly, by toxic products generated during the reaction, or indirectly, by evoking scratching [3,4]. Except for poor body hygiene and environmental exposure (close personal contact, etc), the only predisposing factors that have been identified are systemic immunodeficiency, eg, in patients with acquired immunodeficiency, HTLV-1/HTLV-III infection, or lymphatic leukemia [5-8], and local immunosuppression, eg, topical corticosteroid use [9].

We report a patient with cutaneous T-cell lymphoma who developed a scabies infestation apparently limited to the region of therapeutic irradiation.

Case Report

Clinical Features. An 83-year-old white male with trauma-related T4 paraplegia was diagnosed as having cutaneous T-cell lymphoma with peripheral blood involvement (Sezary’s syndrome), based on peripheral blood smear, bone marrow aspirate/biopsy (June 1997), gene rearrangement studies on peripheral blood that indicated a clonal T-cell process, and abdominal skin biopsy (December 1998). The skin disease began 4 yr previously as a maculopapular erythematous rash of the trunk which progressed to involve the extremities and face (Fig. 1). Microscopically, punch biopsy of abdominal skin demonstrated a dense infiltrate of atypical lymphocytes in the upper dermis with focal epidermotropism, predominantly composed of T-cells, as visualized by immunostaining. The diagnosis of cutaneous T-cell lymphoma was supported by the Departments of Dermatopathology and Hematopathology of the Armed Forces Institute of Pathology.
The patient received five fractionated electron-beam radiation treatments to his upper chest area, completed 23 days before his death. No drug or chemotherapy was initiated. He was cared for in a nursing home, where he developed paraplegia-related decubitus ulcers of the sacrum and foot, sepsis, and acute pneumonia. He died with probable sepsis 6 days after transfer to the Kansas City Veterans Affairs Medical Center.

Pathologic Findings. A complete autopsy demonstrated the patient’s immediate cause of death to be an acute myocardial infarct. In addition to the cutaneous T-cell lymphoma, 3 clinically occult primary carcinomas were identified: invasive adenocarcinoma of the colon, mucinous adenocarcinoma of the prostate, and clear cell carcinoma of the kidney. T-cell lymphoid infiltration consistent with lymphoma was present in the spleen, intraabdominal and cervical lymph nodes, lungs, liver, left kidney, both adrenals, esophagus, and pituitary. Postmortem examination of the skin revealed (in addition to decubitus ulcers) a significant exfoliative erythroderma on the upper chest and neck, and subconfluent erythematous lesions over the legs, abdomen, arms, and face, without tumors or discrete plaques. Approximately 2 cm-long ellipses of skin were removed from the left mid-anterior chest, right mid-anterior chest, and right upper anterior leg for histological examination.

Microscopically, the left and right chest skin were similar in all regards, but the right leg skin was significantly different. In H&E–stained sections, both chest skin samples (Fig. 2a) had multiple intraepidermal organisms characteristic of scabies (*Sarcoptes scabiei*), but the leg skin (Fig. 2b) had no such organisms. All three sites had dermal lymphocytic infiltrates. In both chest skin samples, there was a patchy to mildly dense infiltration by atypical and non-atypical lymphoid cells involving the superficial dermis. In the leg skin, however, there was a patchy to markedly dense infiltration by predominantly atypical lymphoid cells involving the superficial and mid-dermis.

Immunohistochemical staining for T cells (CD-3) and B cells (CD-20) demonstrated the dermal lymphoid infiltration in the chest skin to be approximately 60% T cells and 40% B cells, and that in the leg skin to be about 95% T cells and 5% B cells. Also performed was immunohistochemical staining for S-100 protein (to demonstrate Langerhans cells and melanocytes) and melanocyte-associated antigen recognized by T cells (MART-1) to distinguish the melanocytes from Langerhans cells. The number of high power fields (HPF) counted included chest (autopsy) 187, leg (autopsy) 134, chest (biopsy) 20, and abdomen (biopsy) 13. The stains (Fig. 3) demonstrated fewer melanocytes in the irradiated chest skin samples (1-5/HPF, average 2.8) compared to the non-irradiated leg skin (5-10/HPF, average 7.1), and a notable reduction in Langerhans cells in the irradiated chest skin samples (0-5/HPF, average bilateral chest 1.5, right chest 2.0, left chest 1.2), both lesional and adjacent non-lesional, compared to the non-irradiated leg skin (11-23/HPF, average 17.5). Stains on the abdominal skin biopsy in December 1998 demonstrated melanocytes (5-10/HPF, average 7.4) and Langerhans cells (10-20/HPF, average 13.2) similar to the findings in the leg skin. Stains on a prior right anterior chest skin biopsy in July 1997 demonstrated Langerhans cells (10-22/HPF, average 15.6).

Since the distribution of Langerhans cells can vary within the epidermis of an individual [10], an age/race-matched study of 4 normal anterior chest and 4 normal upper leg skin samples was performed to determine further if the decrease in Langerhans cells was significant. This study demonstrated the numbers of Langerhans cells to be 12.84, 20.54, 18.14, and 10.16/HPF (overall average 15.42) in the 4 normal chest skin samples, and 16.35, 12.36, 10.68, and 23/HPF (overall average 15.59) in the 4 normal leg skin samples.
Fig. 2. Low magnification (x100) of chest and leg skin: (a) chest skin has scabies infestation of the epidermis and a patchy to mildly dense infiltration by atypical and non-atypical lymphoid cells in the superficial dermis; inset (x600). (b) leg skin has no scabies and a patchy to markedly dense infiltration by predominantly atypical lymphoid cells in the superficial and mid dermis; inset (x600).

Fig. 3. Low magnification (x100) of chest and leg skin, stained for S-100 protein: (a) chest skin (irradiated) has relatively few positively staining cells (mostly Langerhans cells, negative for MART-1) in the epidermis; inset (x600). (b) leg skin (non-irradiated) has a considerably greater number of epidermal Langerhans cells; inset (x600).

Fig. 4. Medium power (x200) of biopsy chest skin (non-irradiated) and autopsy chest skin (irradiated), stained for CD1a: (a) the non-irradiated chest skin has a moderate number of positively staining Langerhans cells in the epidermis. (b) the irradiated chest skin has a considerably fewer number of epidermal Langerhans cells (arrows).
Since Langerhans/dendritic cells undergo functional and phenotypic changes following exposure to pathogens [11], an additional marker, CD1a, was used to identify this cell type [12,13], with the following results: autopsy bilateral chest 0-4/HPF (average 1.2, right chest 1.2, left chest 1.4); autopsy leg 12-22/HPF (average 17.6); biopsy (1997) chest 10-21/HPF (average 15.4); and biopsy (1998) abdomen 9-21/HPF (average 13.2). The comparative results of S-100 and CD1a immunostaining are listed in Table 1.

### Table 1. Immunoperoxidase–positive Langerhans cells in patient skin

<table>
<thead>
<tr>
<th>Cells/HPF; mean (and range)</th>
<th>S-100</th>
<th>CD1a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest (pre-radiation)</td>
<td>15.6 (10-22)</td>
<td>15.4 (10-21)</td>
</tr>
<tr>
<td>Chest (post-radiation)</td>
<td>1.5 (0-5)</td>
<td>1.2 (0-4)</td>
</tr>
<tr>
<td>Abdomen (non-radiated)</td>
<td>13.2 (10-20)</td>
<td>13.2 (9-21)</td>
</tr>
<tr>
<td>Leg (non-radiated)</td>
<td>17.6 (11-23)</td>
<td>17.6 (12-22)</td>
</tr>
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Discussion

This patient died from an acute myocardial infarction after long-term medical complications of trauma-related T-4 paraplegia. In addition to 3 clinically occult primary carcinomas (colon, prostate, and kidney) found at autopsy, the patient was diagnosed 4 mo before death to have a fourth malignancy—cutaneous T-cell lymphoma with Sezary’s syndrome. The present report relates to findings associated with local radiation therapy of this cutaneous lymphoma.

At autopsy, the erythroderma of the chest was seen to be much more exfoliative than that of the legs. Histologically, compared to the non-irradiated biopsied leg and abdomen skin samples and autopsy leg skin samples, the irradiated autopsy chest skin sample was infested with scabies, had considerably less dermal infiltration of atypical T cells, and on immunostaining showed many fewer epidermal Langerhans cells. Conclusive interpretation of these findings cannot be made, since multiple chest and leg skin biopsies before and after irradiation were not performed. The clinical and histological evidence, however, strongly suggests that (a) the exfoliative dermatitis and scabies was in the distribution of radiation exposure; (b) the radiation therapy effectively reduced the atypical T-cell lymphocytic infiltrate in the chest skin; and (c) the radiation therapy significantly diminished the number of Langerhans cells in the chest skin.

Comparative studies supporting the validity of the findings included (a) the age/race-matched study of S-100-staining in normal chest and leg skin samples; and (b) immunostaining of the patient’s skin samples by CD1a, a more specific marker for Langerhans cells. The findings in the former study indicate that the number of Langerhans cells in these normal chest and leg skin samples are comparable to the non-irradiated chest and leg skin samples of the above-reported patient. The findings in the latter study indicate that the S-100 and CD1a results are comparable in the autopsy chest and leg skin samples and the biopsy chest and abdomen skin samples (Table 1), and importantly that the post-irradiated (autopsy) chest skin had notably reduced number of Langerhans cells compared to the non-irradiated (biopsy) chest skin.

Although less than conclusive, the above findings offer strong circumstantial evidence that the scabies infestation was associated with the radiation exposure and possibly predisposed to by the consequent diminished epidermal Langerhans cells. Several reported studies support the possibility of a pathogenetic relationship between local cutaneous irradiation, decreased Langerhans cells, and the subsequent development of scabies. (a) It has been demonstrated that X-irradiation of skin as an organ culture in vitro will deplete the tissue of Langerhans cells and/or their surface markers [14,15]. (b) Langerhans cells with their antigen-presenting capacity play a crucial role in immunosurveillance against infections of the skin [16,17]. (c) Systemic immunodeficiency (such as HIV [5], HTLV-1 [6], and HTLV-III [7] infection and lymphatic leukemia [8]) and local immunosuppression (such as topical corticosteroid use [9]) are associated with increased frequency of scabies infection.

Other explanations for the associated findings in the present case should also be considered. Langerhans cells are generally fewer in number in the skin of the trunk compared to that of the extremities [18]. Furthermore, chronic ultraviolet light exposure may decrease the number of Langerhans cells [19]. Immunohistochemical studies on the patient’s chest skin biopsy and abdominal skin biopsy, however, demonstrated a component of Langerhans cells much greater than that found in the post-irradiated chest skin.
In addition, local irradiation could have reduced the number of immunocompetent B-cell and T-cell lymphocytes. Reduction in the number of B cells in the patient's irradiated chest skin was not evident, but a decrease in immunocompetent T cells cannot be excluded, since these cannot be conclusively distinguished from the notably reduced malignant T cells. Additional possible influences not evaluated in this case include cytokines and other factors produced by keratinocytes, fibroblasts, mast cells, endothelial cells, and monocytes/macrophages. Nevertheless, the available evidence indicates that local radiation therapy and probably the reduced number of Langerhans cells predisposed the patient to local infestation with scabies.

Finally, since both scabies and local irradiation are common, it is surprising that this association has not been previously reported. Two possible explanations include (a) most local radiation therapy is deep rather than cutaneous directed; and (b) as in this case, the development of scabies superimposed on cutaneous lymphoma will likely not be clinically detectable, which supports the value of thorough postmortem examination.

Acknowledgements

The authors gratefully acknowledge the Histology Section, Department of Pathology and Laboratory Medicine, Kansas City Veterans Affairs Medical Center, for technical preparations, and Peggy Knaus for assistance in preparing the manuscript.

References