# Variations in presentation of squamous cell carcinoma in situ (Bowen's disease) in immunocompromised patients

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***Background:*** Although cutaneous malignancy is well known to occur at a higher rate in organ transplant recipients, limited data exist regarding the presentation of squamous cell carcinoma (SCC) in situ in patients with immunosuppression from any cause.

***Objective:*** To characterize the presentation of SCC in situ in immunosuppressed patients compared with patients with normal immune function.

***Methods:*** A retrospective comparative university-based study, reviewing charts with histologically confirmed Bowen's disease diagnosed between January 1999 and January 2003.

***Results:*** Two hundred ninety-nine patients (193 men, 106 women) with 407 SCC in situ tumors were included. Fifty-seven patients (19%) were immunocompromised, including 43 organ transplant recipients, 7 patients with acute and chronic leukemia, and 6 patients with immune-suppressing infections or autoimmune disease. Immunocompromised patients were significantly younger (mean, 61.7 years) than non-immunocompromised patients, 72.6 years, $P < .0001$) and were more often male ($P = .0115$). Immunocompromised patients were significantly more likely to have multiple SCC in situ tumors (33% vs 15%; $P = .012$). Immunocompromised patients were also more likely to present with tumors on the trunk and extremities (odds ratio [OR], 2.03; $P = .0019$) and particularly on the neck (OR 3.7; $P = .00075$) than were non-immunocompromised patients. Overall, 11 patients (3.7%) developed a histologically confirmed recurrence of SCC in situ after apparently adequate surgical treatment. The rate of recurrence was higher in immunocompromised (9%) than in non-immunocompromised patients (3%; $P = .039$).

***Limitations:*** The mean follow-up duration of 35 months may underestimate the recurrence rate.

***Conclusions:*** Immunocompromised patients are at significant risk of SCC in situ, and SCC in situ in this population is likely to occur multiply and behave more aggressively. Close dermatologic surveillance of these patients is warranted. (J Am Acad Dermatol 2008;59:68-71.)

## INTRODUCTION

Squamous cell carcinoma (SCC) in situ (Bowen's disease) is an intraepidermal malignancy most commonly found on sun-exposed skin of the head, neck, and extremities.[1] SCC in situ has a rate of advancement to invasive SCC of up to 5%.[2] Risk factors for Bowen's disease include fair skin, long-term sun-damage, radiation exposure, immune compromise and human papillomavirus infection.[1,3-5] A variety of surgical and nonsurgical treatment modalities are employed, with a 5-year recurrence rate between 2.5% and 19%.[2]

Cutaneous malignancy is well known to occur at a higher rate in immune-suppressed patients. Organ

*Abbreviations used:*

CLL: chronic lymphocytic leukemia
NMSC: nonmelanoma skin cancer
OTR: organ transplant recipient
SCC: squamous cell carcinoma

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transplant recipients (OTRs) are at higher risk of nonmelanoma skin cancer (NMSC), particularly SCC.[6] Previous studies have shown an incidence of NMSC of 24% to 43% in patients 10 years after organ transplant.[7,8] Patients with other forms of immune suppression, including those with chronic leukemias, immune-suppressing infections, and those taking long-term immune-suppressive medications for autoimmune diseases also appear to be at increased risk of NMSC.[9,10] SCC in this diverse population of immune-suppressed patients is more likely to be clinically aggressive, with a higher rate of metastasis and recurrence.[9-11] Progression from in situ malignancy to invasive disease may occur at a higher rate in such patients. Most reports studying the presentation of NMSC in immune-suppressed patients have focused on a particular cause of immune suppression and on invasive SCC. We were interested in characterizing the presentation of SCC in situ in patients with any cause of immunosuppression compared to patients with normal immune function.

## MATERIAL AND METHODS

We obtained institutional review board approval from our hospital's ethics committee to review our academic institution's database for histologically confirmed cases of primary cutaneous SCC in situ diagnosed from January 1999 to January 2003 with at least 12 months of clinical follow-up. Because of potentially confounding variables, lesions with features of human papillomavirus-association on routine histology, found on mucous membranes, or found within or at the margins of invasive SCC were excluded.

The parameters studied included age and sex of the patient, comorbid medical conditions, site and size (largest diameter) of the lesion at biopsy, previous treatment of the lesion, and history of other skin cancers or skin cancer precursors. Recurrence was defined as histologically-confirmed SCC in situ developing within the surgical scar of a previously treated SCC in situ excised with histologically clear margins. Immunocompromised patients were defined as those who were organ transplant recipients, HIV positive, who routinely took immunosuppressive medications (including prednisone, azathioprine, methotrexate, and infliximab), and/or who had been diagnosed with acute myelogenous leukemia, chronic lymphocytic leukemia (CLL), combined-variable immunodeficiency, metastatic cancer, rheumatoid arthritis, or systemic lupus erythematosus.

Data were assembled and compared statistically with the Student *t* test or chi-square test as appropriate using computer software (SAS for Windows). Odds ratios (ORs) with 95% confidence intervals (CI) were similarly calculated with computer software. A *P* value less than .05 was considered statistically significant. No adjustment of the *P* value was made to account for multiple comparisons.

## RESULTS

Two hundred ninety-nine patients with 407 lesions were included in this study (Table I). Men constituted 64.5% of the patients (193/299) and 34.5% were women (106/299). The average age was 69.8 years (range, 33-99 years). Fifty-seven patients (19%) with SCC in situ were considered immunocompromised. This group included the following patients: those with kidney transplants (n = 24), cardiac organ transplants (n = 12), CLL (n = 6), liver transplant (n = 3), HIV/AIDS (n = 3), kidney and pancreas transplant (n = 2), metastatic breast cancer (n = 1), cardiac organ and kidney transplant (n = 1), kidney and lung transplant (n = 1), acute myelogenous leukemia (n = 1), rheumatoid arthritis (n = 1), systemic lupus erythematosus (n = 1), and combined variable immunodeficiency (n = 1). Three fourths (43/57) of the immunocompromised patients were OTRs. A significantly greater proportion of immunocompromised patients were male (45/57, 79%) compared with non-immunocompromised patients (48/242; 61%; $P$ = .0115). immunocompromised patients with SCC in situ were significantly younger (mean, 61.7 years; median, 63 years) than non-immunocompromised patients with SCC in situ (mean, 72.6 years; median, 74 years; $P < .0001$). Mean lesion size did not vary among the immunocompromised and non-immunocompromised populations.

Of the 299 patients, 55 had multiple lesions during the study period (see Table I). Immunocompromised patients were significantly more likely than non-immunocompromised patients to have multiple SCC in situ tumors. One third of immunocompromised patients (19/57) had two or more lesions, compared with 15% (36/242) of non-immunocompromised patients ($P$ = .012). Immunocompromised patients were also significantly more likely to have 3 or more lesions (12/57, 21%; $P$ = .000197), 4 or more lesions (8/57, 14%; $P$ = .00013), and 5 or more lesions (5/57, 9%; $P$ = .00756). There were no significant differences between SCC in situ variables based on underlying cause of immunosuppression.

Overall, 11 patients (3.7%) developed a histologically confirmed recurrence of SCC in situ after apparently adequate surgical treatment, after a mean follow-up duration of 35 months (see Table I). The rate of recurrence was higher in immunocompromised patients (n = 5; 9%) than in non-immunocompromised patients (n = 6; 3%; $P$ = .0389).