ORIGINAL ARTICLE

The risk of melanoma and hematologic cancers in patients with psoriasis

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Background: The risk of melanoma and hematologic cancers in patients with psoriasis is controversial.

Objective: We sought to assess the risk of melanoma and hematologic cancers in patients with psoriasis, and the association with different treatments.

Methods: We used case-control and retrospective cohort designs to determine melanoma or hematologic cancer risk in patients with psoriasis. Risk with treatment type was assessed using Fisher exact test.

Results: Patients with psoriasis had 1.53 times greater risk of developing a malignancy compared with patients without psoriasis ($P < .01$). There were no significant differences in malignancy risk among patients treated with topicals, phototherapy, systemics, or biologic agents. Patients with psoriasis and malignancy did not have significantly worse survival than patients without psoriasis.

Limitations: It is possible that patients developed malignancy subsequent to the follow-up time included in the study.

Conclusion: Patients with psoriasis may experience an elevated risk of melanoma and hematologic cancers, compared with the general population. The risk is not increased by systemic or biologic psoriasis therapies. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.09.047.)

Key words: biologic; hematologic cancer; malignancy; melanoma; phototherapy; psoriasis; topical therapy.

There is a controversial risk of malignancy in patients with psoriasis.[1-3] Although the chronic inflammatory state observed in psoriasis may induce protumorigenic effects, treatments for psoriasis such as ultraviolet (UV) light, systemic therapy, and tumor necrosis factor (TNF)-alfa therapy[4-8] may also place patients with psoriasis at greater risk for cancers. TNF-alfa may be particularly integral to stimulating the immune response to melanoma and other cancers.[9]

Prior studies have suggested increased risks for skin and hematologic cancers in patients with

Abbreviations used:

CCI:	Charlson comorbidity index
CI:	confidence interval
HR:	hazard ratio
IL:	interleukin
KPSC:	Kaiser Permanente Southern California
PUVA:	psoralen plus ultraviolet A
RA:	rheumatoid arthritis
RR:	rate ratio
TNF:	tumor necrosis factor
TNFi:	tumor necrosis factor inhibitor
UV:	ultraviolet

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psoriasis.[1,2] These risks are controversial. Margolis et al[1] provided the most compelling evidence of this risk, which was attributed to nonmelanoma skin cancers and hematologic cancers. Other studies in patients with psoriasis have also found an increased risk for melanoma in patients treated with psoralen plus UVA (PUVA).[5] The risk for cancers in patients with psoriasis treated with systemic therapies is less well-characterized. One study in patients with rheumatoid arthritis (RA) suggests a heightened risk for melanoma in patients treated with TNF-alfa inhibitors.[10] Other studies have not observed this risk for melanoma or hematologic cancers in patients with RA, inflammatory bowel disease, or psoriasis treated with TNF inhibitors (TNFi).[3]

CAPSULE SUMMARY

- Previous studies have suggested increased risks for skin and hematologic cancers in patients with psoriasis.
- Patients with psoriasis experience an increased risk of melanoma and hematologic malignancy although this risk is not mediated by psoriasis therapy.
- Patients with psoriasis and malignancy do not experience worse survival than patients without psoriasis.

In this large cohort study, which provides a markedly diverse population, we examine the risk of melanoma and hematologic cancers in patients with psoriasis, especially those treated with phototherapy and systemic therapy. Examining this issue in a large, diverse cohort will aid in characterizing the complexity of psoriasis as a multisystemic disorder.

METHODS

We used case-control and retrospective cohort designs to examine patients with melanoma or hematologic cancer with and without a diagnosis of psoriasis.

Cohort selection

Kaiser Permanente Southern California (KPSC) health plan is a large, integrated health maintenance organization that served approximately 3.2 million members during each of the past 10 years, approximately 15% of southern California's population. Member demographic, socioeconomic, and racial/ethnic composition are representative of California. KPSC members receive the large majority of their care through KPSC-owned facilities, making this cohort notably apprised of health maintenance follow-up and providing true estimates of second events after primary disease. Objective clinical data from this system are collected and stored in rigorously maintained databases, rendering information largely reliable and robust.

KPSC members with *International Classification of Diseases, Ninth Revision* diagnostic codes for psoriasis (696.1), melanoma (172.0-9), and hematologic cancers (202.8-9, 204.0-1, 205.0-1, 200.0-8, 201, 202.0-7, 203.0, 206, 207.0-2, 208) were examined. Only patients with at least 1 year of continuous enrollment with at least 1 medical encounter from January 1, 2004, to December 31, 2013, were included.

Patients were classified as having psoriasis if at least 3 visits with the primary diagnosis as "psoriasis" occurred within this time period. Patients who did not meet these criteria were excluded. Patients who had melanoma or hematologic cancers before the third visit for psoriasis were excluded (Supplemental Fig 1).

Each patient with psoriasis was also assigned to 1 of 4 mutually exclusive treatment cohorts: (1) TNFi cohort: patients who received etanercept, infliximab, or adalimumab for at least 2 consecutive months, regardless of use combined with an oral agent or phototherapy; (2) oral therapy cohort: patients who received oral agents (ie, cyclosporine, acitretin, or methotrexate) as their highest level therapy; (3) phototherapy cohort: patients who received phototherapy (broadband UVB, narrowband UVB, or PUVA) as their highest level therapy; and (4) topical cohort: patients who were not treated with TNFi, oral agents, or phototherapy, but who were treated with topical agents.

Overall survival (OS) was assessed by linking data from the California State Death Registry to KPSC records.

Statistical analysis

Melanoma or hematologic cancers among patients with and without psoriasis. We used a case-control design to compare characteristics between all patients in the cohort with and without psoriasis using Fisher exact tests. We also compared the instance rate of melanoma or hematologic cancers among these patients.

Melanoma or hematologic cancers among patients with and without psoriasis using matched cohort. A retrospective cohort study was used to create a cohort of age- and sex-matched patients without psoriasis in a 1:4 ratio who were followed up from time of diagnosis of psoriasis for the psoriasis cohort. The matched cohort was pooled from KPSC patients with diagnoses of melanoma or hematologic cancers. The