Outpatient Dermatology Consultation Impacts the Diagnosis and Management of Pediatric Oncology Patients: A Retrospective Study

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Scholarly Report submitted in partial fulfillment of the MD Degree at Harvard Medical School

Date: 3 February 2018

Student Name: Hannah Song, BA

Scholarly Report Title: Outpatient dermatology consultation impacts the diagnosis and management of pediatric oncology patients: A retrospective study

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Collaborators, with Affiliations: Sarah N. Robinson, MD, Harvard Combined Dermatology Residency Program

TITLE: Outpatient dermatology consultation impacts the diagnosis and management of pediatric oncology patients: A retrospective study

Hannah Song, Sarah N. Robinson, Jennifer T. Huang

Purpose: There are limited data on the impact of dermatology involvement on the care of pediatric oncology patients. Prior studies of the epidemiology of skin conditions and the role of dermatologists in the care of pediatric patients were not specific to the pediatric oncology population. The objectives of this study were to determine the characteristics of outpatient dermatology visits and the resulting impact on diagnosis and management of pediatric oncology patients.

Methods: The medical records of all patients with a Dana-Farber Cancer Institute medical record number and a dermatology clinic visit at Boston Children's Hospital from 2008 to 2015 were retrospectively reviewed for demographic and medical information. Change in diagnosis was defined as discordance between dermatology and oncology assessment of the skin condition. Change in management was defined as the addition, withdrawal, or change in dose of topical or systemic medication.

Results: The most common dermatologic diagnoses in 516 patients were skin infections (21.3%) and nonmalignant skin eruptions (33.4%). A diagnosis of significant impact (ie, malignancy, adverse cutaneous drug reaction, graft-versus-host disease, varicella-zoster virus, or herpes simplex virus infection), was made at the dermatology clinic in 14.7% of visits. Consultation resulted in a change in diagnosis in 59.8% of patients, change in dermatologic management in 72.4% of patients, and change in management of noncutaneous issues in 12.4% of patients.

Conclusions: Outpatient dermatology consultation can affect the care of pediatric oncology patients, including the diagnosis and treatment of skin conditions and management of nondermatologic issues.

Contribution to work:

I executed the study design, data collection, data analysis, and manuscript preparation and submission under the supervision of Dr. Jennifer T. Huang. Dr. Huang's initial interest was a state-of-the art article regarding the multidisciplinary brain tumor clinic at Dana-Farber clinic to emphasize the importance of dermatology input on the care of pediatric oncology patients. During my research year, I also saw many instances where dermatologic care impacted the care of pediatric oncology patients, and wanted to study this observation in a more systematic manner. Ultimately, we decided upon pursuing a study with the following objectives: a description of the dermatologic conditions seen in pediatric oncology patients, and more importantly, the impact of dermatology consultation on the diagnosis and management of pediatric oncology patients. I submitted the data request for the list of pediatric oncology patients seen by dermatology, reviewed 1001 charts and applied our inclusion and exclusion criteria, and established a cohort of 516 pediatric oncology patients seen by dermatology from 2008 to 2015. I reviewed the 516 charts, and discussed all cases where I was unclear regarding changes in diagnosis or management on a case-by-case basis with Dr. Huang. Then, I analyzed the descriptive data using RedCAP and wrote my initial draft. Dr. Huang and Dr. Sarah N. Robinson provided invaluable input in editing the rough draft and provided critical revisions for the final draft that we submitted to the Journal of the American Academy of Dermatology, which went through several rounds of revisions before being accepted for publication.

Citation

Song, H, Robinson, SN, Huang, JT. "Outpatient dermatology consultation impacts the diagnosis and management of pediatric oncology patients: A retrospective study." *Journal of the American Academy of Dermatology*. 2017, Nov. 77(5): 879-885.

Appendix:

Outpatient Dermatology Consultation Impacts the Diagnosis and Management of Pediatric Oncology Patients: A Retrospective Study

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Conflicts of Interest Disclosure: None declared.

Institutional Review Board Approval: The Institutional Review Board at Boston Children's Hospital approved this study. IRB-P00016307.

Author Contributions: Ms. Hannah Song had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior presentations: This work was presented at the Society of Investigative Dermatology as an oral presentation in Portland, Oregon in April, 2017.

Word Count: Abstract: 162/200; **Capsule summary:** 44/50; **Text:** 1937/2500

Number of tables: 4; **Number of figures:** 2; **Number of references:** 24

Abstract:

Background: The impact of dermatology consultation on the care of children with oncologic conditions is unknown.

Objective: To review outpatient dermatology visits and the resulting impact on diagnosis and management of pediatric oncology patients.

Methods: Retrospective review of pediatric oncology patients with outpatient dermatology visits at a tertiary care center from 2008-2015.

Results: The most common dermatologic diagnoses in 516 patients were skin infections (21.3%) and nonmalignant skin eruptions (33.4%). A diagnosis of significant impact, i.e., malignancy, cutaneous drug eruption, graft versus host disease, varicella zoster or herpes simplex virus infection, was made at the dermatology clinic in 14.7% visits. Consultation resulted in a change in diagnosis in 59.8%, dermatologic management in 72.4% and management of non-cutaneous issues in 12.4% patients.

Limitations:

Use of electronic medical records, non-generalizable study population, and retrospective design represent potential limitations.

Conclusion:

Outpatient dermatology consultation can impact the care of pediatric oncology patients, with respect to diagnosis and treatment of skin conditions, and management of non-dermatologic issues.

Capsule Summary:

- Pediatric oncology patients develop skin conditions including drug eruption, graft-versus-host disease, cutaneous infection, and malignancy.
- Outpatient dermatology consultation resulted in a change in diagnosis in 59.8% and change in management in 72.4% of clinic visits.
- Dermatology consultation impacts the care of pediatric oncology patients.

Key words: pediatric oncology, treatment, management, epidemiology, outpatient visits

Introduction:

Advancements in oncologic therapy have reduced mortality rates from primary disease.¹

Correspondingly, reactions and complications from cancer therapy have increased, as well as the need for long-term surveillance for secondary neoplasms, especially in pediatric patients.^{1 2 3 4}

There are limited data on the impact of dermatology involvement on the care of these children.

Prior studies of the epidemiology of skin conditions and the role of dermatologists in the care of pediatric patients were not specific to the pediatric oncology population.^{5 6 7}

The objectives of this study were to determine the characteristics of outpatient dermatology visits and the resulting impact on diagnosis and management of pediatric oncology patients.

Methods:

Overview

The medical records of all patients with a Dana-Farber Cancer Institute medical record number and a dermatology clinic visit at Boston Children's Hospital from 2008-2015 were retrospectively reviewed for demographic and medical information. Inclusion criteria included an oncologic diagnosis and/or diagnosis requiring hematopoietic stem cell transplant (HSCT) and a dermatology visit from 2008-2015. Exclusion criteria included the absence of a dermatology visit after an oncologic diagnosis was made. Institutional review board approval was obtained through the Boston Children's Hospital (P00016307).

Data collection

Each medical record was reviewed for demographic and clinical information including age, sex, race, distance from home to hospital, and cancer type and therapy. Dermatologic assessment and management including treatment and procedures were recorded from up to four visits for unique dermatology complaints in each patient. When there were multiple cutaneous findings (e.g., atopic dermatitis and molluscum contagiosum), all diagnoses were included.

If available, preliminary assessment and management of the skin condition by the referring oncologist were recorded. Time from referral by the oncology service to dermatology clinic appointment was recorded.

Study definitions

Change in diagnosis was defined as discordance between dermatology and oncology assessment of the skin condition. Oncology referrals for routine skin surveillance, in which the dermatologist documented benign melanocytic nevi, were categorized separately as "skin surveillance."

Change in dermatologic management was defined as the addition, withdrawal, or change in dose of topical or systemic medication for a dermatologic condition. Change in medical management was defined as the addition, withdrawal, or change in dose of a systemic medication, or procedure for a non-dermatologic condition. When the oncologist documented a need for dermatology consultation regarding medications or procedures for non-dermatologic issues, we categorized the subsequent dermatology visit as leading to a change in medical management.

Changes in dermatologic and medical management were examined for all referrals from oncology.

Diagnoses of significant impact were defined as cutaneous drug reaction, cutaneous malignancy, herpes simplex virus (HSV) or varicella zoster virus (VZV) infection, and graft-versus-host (GVHD) due to their potential for altering oncologic therapy.

Data analysis:

Descriptive statistical analysis was performed, with categorical data provided as frequencies and percentages, and continuous data provided as means with standard deviations, and median values with ranges. Comparative statistical analysis was performed using unpaired t-test and two-tailed Fisher's test, utilizing GraphPad software.

Results:

There were 1001 unique pediatric oncology patients seen by dermatologists from 2008-2015.

The method of cohort selection is demonstrated in Figure 1. The medical records of 516 patients who met inclusion and exclusion criteria were reviewed for demographic and clinical information. The medical records of 251 oncology patients with documented oncology referral and subsequent dermatology clinic visit were reviewed for the impact of dermatology consultation on diagnosis and treatment.

Demographic features

The demographic features of pediatric oncology patients seen in the dermatology clinic from 2008-2015 are summarized in Table 1. Patients were evenly distributed by age and sex.

Clinical characteristics and dermatologic diagnoses

The oncologic characteristics are summarized in Table 2. In 516 patients, hematologic (43.4%; 224) and brain (12.8%; 66) malignancies represented the most common primary diagnosis. The most common treatment regimens included: HSCT $\pm$ other oncologic therapy (38.6%; 199), chemotherapy (27.7%; 143), and combination chemotherapy and radiation (21.3%; 110).

The mean time from cancer diagnosis to dermatology visit was 65.2 months for routine skin screening. There was a significantly increased mean time from oncology referral to initial dermatology visit of 68.6 (SD=90.2) days for routine skin screening, compared to 19.8 (SD=34.1) days for a specific cutaneous complaint ($p<0.001$).

The most common reasons for initial consultation were skin issue after cancer therapy in 59.1% (305/516) and skin cancer surveillance in 38.8% (200/516) patients. Only 6.2% (32) patients were referred prior to cancer therapy initiation. A significantly higher proportion of HSCT recipients was referred for routine skin cancer surveillance, compared to patients who received other treatment regimens (26.1% vs. 12.0%; $p<0.0001$).

The dermatologic characteristics are summarized in Table 3. Dermatology consultation resulted in 827 diagnoses made during 743 visits, including skin infections in 21.3% (176), cutaneous drug effect in 5.4% (45), cutaneous GVHD in 4% (33), and malignant lesion in 4.1% (34).

The most common infections were viral and bacterial, which accounted for 66.5% (117/176) and 14.2% (25/176) of infections, respectively. Molluscum contagiosum and/or verruca vulgaris accounted for 89.7% (105/117) of viral infections, while more concerning infections, including HSV or VZV, accounted for 4.3% (5/117). There was one deep invasive fungal infection.

Of 45 cases of cutaneous drug adverse effects, 26.7% (12) required temporary or permanent cessation of therapy: drug hypersensitivity reaction (not otherwise specified) (3), morbilliform drug rash (2), voriconazole-induced pseudoporphyria or photosensitivity (2), linear immunoglobulin A dermatosis secondary to vancomycin (1), drug reaction with eosinophilia and systemic symptoms (DRESS) (1), acneiform eruption induced by cetuximab (1), psoriasiform eruption due to sorafenib (1), and methotrexate-induced ultraviolet radiation recall dermatitis (1). Of patients with GVHD, 90.9% (30/33) were diagnosed with chronic cutaneous GVHD.

Malignant dermatologic diagnoses included: squamous cell carcinoma (16), basal cell carcinoma (5), leukemia cutis or cutaneous lymphoma (4), dermatofibrosarcoma protuberans (3), melanoma (2), cutaneous neuroblastoma (1), giant cell fibroblastoma (1), infantile fibrosarcoma (1), and Langerhans cell histiocytosis (1).

Other diagnoses were 1) skin eruptions (e.g., atopic dermatitis, psoriasis, seborrheic dermatitis) in 33.4% (276/827) of visits; 2) skin lesions (e.g., congenital nevi, acrochordon, seborrheic keratosis) in 20.3% (168/827); and 3) miscellaneous diagnoses (predominantly changes in hair

and nails) in 11.5% (95/827).

A total of 118 skin biopsies were performed. Histopathology yielded a definitive diagnosis in 87.3% (103/118): 9.3% (11/118) biopsies were consistent with atypical nevi, and 28.8% (34/118) were consistent with malignancy.

Impact on Care of Pediatric Oncology Patients

There were 251 pediatric patients with an initial oncology referral to dermatology from 2008-2015. Details regarding changes in diagnosis and management are listed in Table 4. At the initial visit, dermatology consultation resulted in a change in diagnosis at 59.8% (150/251) visits. Diagnoses of significant impact made in 14.7% (22/150) included cutaneous drug reaction in 9.3% (14/150), malignant lesion in 2% (3/150), HSV/VZV in 2% (3/150), and GVHD in 1.3% (2/150) patients.

In 20.3% (51/251) cases, the referring oncologist was concerned about a diagnosis of significant impact, including an atypical or malignant lesion in 7.6% (19/251), cutaneous drug adverse effect in 6.4% (16/251), GVHD in 5.6% (14/251), and HSV or VZV in 0.8% (2/251). The evaluating dermatologist provided an alternative, reassuring diagnosis in 43.1% (22/51) of these cases.

Overall, there was a change in management of dermatologic disease in 72.4% of patients.

Change in management was made in 70% (105/150) of visits at which there was a change in

diagnosis, and in 77.6% (52/67) at which there was no change in diagnosis. The most frequent change in management was the addition of a topical agent (Table 4).

Dermatology consultation resulted in changes in medical management in 12.4% (31/251) of visits including: reassurance to continue systemic therapy in 51.6% (16/31), delay and/or cessation of systemic therapy in 16.1% (5/31), prevention of unnecessary systemic therapy in 9.7% (3/31), initiation of systemic therapy in 9.7% (3/31), and reassurance to continue procedures in 12.9% (4/31).

During the study period, there was a 72.6% increase in the number of unique pediatric oncology patients seen in the dermatology clinic, and 82.5% increase in total number of dermatology visits by pediatric oncology patients (Fig 2).

Discussion

Dermatology evaluation impacts the care of pediatric oncology patients by changing the diagnosis and management of cutaneous disease. Previous studies have demonstrated that dermatologists outperform generalists in making common skin diagnoses^{8 9 10 11} Our results suggest that pediatric dermatologists similarly improve diagnostic accuracy, allowing for timely and appropriate intervention in the pediatric oncology population. Pediatric oncology patients have a high burden of disease long after treatment completion.¹² Rare diagnoses may occur, and common cutaneous conditions may have severe and/or atypical presentations. Diagnostic accuracy has the potential to improve the quality of care.

Dermatology consultation may impact medical management of non-cutaneous issues that have important implications for cancer therapy. Examples of changes in medical management in our study included: reassurance to continue systemic therapy (e.g., symptomatic management of a cutaneous drug adverse effect that allowed for continuation of chemotherapy), delay of systemic therapy (e.g., diagnosis of severe Coxsackie A6 infection that resulted in temporary cessation in chemotherapy), or reassurance to continue a procedure (e.g., diagnosis of arthropod assault when surgery was almost cancelled due to new rash of unknown etiology).

The importance of dermatologic involvement in the diagnosis of malignant disease in pediatric oncology patients may be underrecognized. Cutaneous involvement of visceral or hematologic malignancies in children may present as extramedullary hematopoiesis, leukemia cutis or Langerhans cell histiocytosis.^{13 14 15 16} Pediatric cancer survivors are at increased risk for melanoma and nonmelanoma skin cancer, even during childhood.^{17 18} In our cohort, primary cutaneous or non-cutaneous malignancy accounted for 4.1% of diagnoses and 28.8% of skin biopsies; a higher degree of suspicion for rare or malignant diagnoses is necessary in this population.

In addition to diagnosis of malignant disease, our study found that dermatologists made a variety of other diagnoses requiring prompt intervention, i.e., cutaneous drug side effect, GVHD, HSV or VZV, in 12.7% of initial visits where the oncologist had not considered these diagnoses. Dermatologists also play an important role by managing nonmalignant yet symptomatic disease and by providing reassurance to both patients and providers. The high frequency of common

dermatologic diagnoses such as molluscum contagiosum and verruca vulgaris suggests that dermatologists should be trained to manage "benign" viral infections in this population.

Oncologists at our institution recognize the need for skin surveillance in high-risk populations, as demonstrated by the frequent referral of HSCT patients for skin cancer surveillance. HSCT patients, particularly those with chronic GVHD, are at increased risk for skin cancer, and require closer surveillance.^{22 23 24 25} Long-term follow up guidelines currently recommend annual skin exams for HSCT recipients.²⁶

There is a concerted, collaborative effort to address dermatologic complaints in pediatric oncology patients in a timely manner at our institution. Although previous studies have highlighted long wait times ranging from 9.0-12.7 weeks,^{23 24} we found shorter wait times for patients presenting for both a specific cutaneous complaint and routine skin screening. The 72% increase in unique pediatric oncology patients seen at the dermatology clinic from 2008-2015 suggests a recognition of the value of dermatology input.

Our findings must be interpreted in the context of the study design. This was a single-center retrospective study at a pediatric tertiary academic center, and the study population may not be generalizable. The variation in documentation in medical records inherent to the retrospective design limited our ability to capture all referrals from oncology.

Conclusion:

Dermatology consultation in the outpatient setting impacts the care of pediatric oncology patients. Dermatologists can diagnose common nonmalignant cutaneous conditions, which may have severe or atypical manifestations, recognize more concerning, rare conditions including cutaneous malignancies, and provide useful and collaborative input for critical medical decisions. There should be a low threshold to involve dermatology in the care of this unique population.

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Abbreviations:

HSCT=hematopoietic stem cell transplant; GVHD= graft-versus-host; HSV=herpes simplex virus; VZV=varicella zoster virus

Figure Legends:

Figure 1. Patient selection of pediatric oncology patients seen by dermatology between 2008-2015

Figure 2. Increase in total visits and unique number of pediatric oncology patients seen by dermatology between 2008-2015

Table 1. Demographic features of pediatric oncology patients seen by dermatology between 2008-2015 (n=516)

Characteristic	Number (%)
Sex	
Male	282 (54.7)
Female	234 (45.3)
Age at first dermatology visit	
0-5	154 (29.8)
6-12	171 (33.1)
13-18	153 (29.7)
>18	38 (7.4)
Race	
White	355 (68.8)
Hispanic	65 (12.6)
Middle Eastern	27 (5.2)
Black	23 (4.5)
Asian	17 (3.3)
Native American	1 (0.2)
Not available	28 (5.4)
Distance to Hospital	
<50 miles	342 (66.3)
50-100 miles	89 (17.2)
100-500 miles	54 (10.5)
>500 miles	31 (6.0)

Table 2. Oncologic characteristics of pediatric oncology patients seen in dermatology clinic between 2008-2015 (n=516)

Clinical Characteristic	Number (%)
Primary oncologic diagnosis	
Hematologic	224 (43.4)
Brain	66 (12.8)
Neuroblastoma	31 (6.0)
Bone tumor (Ewing, osteosarcoma)	27 (5.2)
Langerhans cell histiocytosis	23 (4.5)
Melanoma	9 (1.7)
Wilm's tumor	8 (1.6)
Other non-cutaneous	64 (12.4)
Other cutaneous	9 (1.7)
Other diagnosis leading to HSCT	67 (13.0)
Treatment	
Surgery only	47 (9.1)
Chemotherapy +/- surgery	143 (27.7)
Radiation +/- surgery	8 (1.6)
Chemotherapy + radiation +/- surgery	110 (21.3)
Hematopoietic stem cell transplant	199 (38.6)
No treatment	9 (1.7)

Table 3. Dermatologic characteristics of pediatric oncology patients between 2008-2015 (n=516)

Clinical Characteristic	Number (%)
Reason for initial consultation	
Baseline screening	32 (6.2%)
Skin issue during treatment	92 (17.8%)
Skin issue after treatment	305 (59.1%)
Skin cancer surveillance	200 (38.8%)
Dermatology diagnosis	
Skin infection	176 (21.3)
<i>Bacterial</i>	25 (3)
<i>Viral (VZV, HSV)</i>	5 (0.6)
<i>Viral (Warts, Molluscum)</i>	105 (12.7)
<i>Viral (Other)</i>	7 (0.8)
<i>Fungal</i>	22 (2.7)
<i>Other</i>	12 (1.5)
Cutaneous drug side effect	45 (5.4)
Malignant lesion	34 (4.1)
Cutaneous GVHD	33 (4.0)
Other skin eruption *	276 (33.4)
Other skin lesion**	168 (20.3)
Other ***	95 (11.5)
Skin biopsy	
# of skin biopsies	118
# resulting in definitive diagnosis	103/118 (87.3)
# of malignancies	34/118 (28.8)
# of atypical nevi	11/118 (9.3)

*Common diagnoses: atopic dermatitis, irritant dermatitis, contact dermatitis, seborrheic dermatitis, psoriasis, acne, keratosis pilaris

**Common diagnoses: acrochordon, congenital nevus, dermatofibroma, seborrheic keratosis, cysts, atypical nevi

*** Common diagnoses: alopecia, nail dystrophy and/or other changes, scars

Table 4. Dermatologic management of pediatric oncology patients between 2008-2015 (n=251)

Characteristic	Number (%)
Diagnosis by dermatology compared to oncology	
Same	67 (26.7)
Different	150 (59.8)
Routine skin exam	34 (13.5)
Overall change in management	
Yes	157 (72.4)
No	60 (27.6)
Change in management of dermatologic condition when specialties had different diagnoses	
Yes	105/150 (70)
No	45/150 (30)
Type of change in dermatologic management	
Add topical medication	77/105 (73.3)
Withdraw topical medication	5/105 (4.8)
Add oral medication	9/105 (8.6)
Withdraw oral medication	1/105 (1.0)
Other	33/105 (31.4)
Change in management of dermatologic condition when both specialties had same diagnosis	
Yes	52/67 (77.6)
No	15/67 (22.4)
Type of change in dermatologic management	
Add topical medication	46/52 (88.5)
Withdraw topical medication	12/52 (23.1)
Add oral medication	6/52 (11.5)
Withdraw oral medication	0/52 (0)
Other	10/52 (19.2)
Change in medical management	
Yes	31/251 (12.4)

No	220/251 (87.6)
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Type of change in medical management

Reassurance to continue systemic therapy	16/31 (51.6)
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Delay/stop systemic therapy	5/31 (16.1)
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Prevent unnecessary systemic therapy	3/31 (9.7)
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Initiate systemic therapy	3/31 (9.7)
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Reassurance to continue procedure	4/31 (12.9)
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