Published in final edited form as:

Int J Dermatol. 2019 June ; 58(6): 707–712. doi:10.1111/ijd.14305.

A retrospective review of patients with Kaposi's sarcoma in Botswana

Christa Slaughter, MD¹, Victoria Williams, MD^{2,3}, Surbhi Grover, MD^{4,5}, Elizabeth Bigger, MD⁶, Mukendi Kayembe, MD^{7,8}, Sebathu Chiyapo, MD⁵, Nicholas J. Jackson, PhD, MPH⁹, Scott Dryden-Peterson, MD^{10,11,12}, Carrie L. Kovarik, MD³, Karolyn A. Wanat, MD¹³

¹Department of Dermatology, Oregon Health and Sciences University, Portland, OR, USA,

²Ministry of Health of Botswana, Gaborone, Botswana,

³Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA,

⁴Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA, USA,

⁵Department of Oncology, Princess Marina Hospital, Gaborone, Botswana,

⁶Department of Medical Oncology, Massachusetts General Hospital, Boston, MA, USA,

⁷Department of Anatomical Pathology, National Health Laboratory, Gaborone, Botswana,

⁸Department of Pathology, University of Botswana School of Medicine, Gaborone, Botswana,

⁹Department of Medicine Statistics Core, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, USA,

¹⁰Division of Infectious Diseases, Brigham and Women's Hospital, Boston, MA, USA,

¹¹Botswana Harvard AIDS Institute, Gaborone, Botswana,

¹²Harvard T. H. Chan School of Public Health, Boston, MA, USA,

¹³Department of Dermatology and Pathology, University of Iowa, Iowa City, IA, USA

Abstract

Background—Despite widespread antiretroviral coverage in Botswana, Kaposi's sarcoma (KS) remains among the most common malignancies. To date, adult KS in Botswana is not well characterized. The diagnosis relies on clinical suspicion that is often confirmed by histopathology given the implications of treatment; however, this poses a significant resource burden.

Methods—We conducted a retrospective review of the cohort of patients biopsied for possible KS at Princess Marina Hospital, the main dermatology referral site in Botswana, from September 2008 through June 2015 to describe the demographics, human immunodeficiency virus (HIV) characteristics, and clinical presentations of these patients. Histopathologic diagnoses were

Correspondence: Christa Slaughter, MD, 3303 SW Bond Ave #16, Portland, OR 97239, USA, christaslaughter@gmail.com.

Conflicts of interest: None declared.

reviewed, and positive predictive value (PPV) was used to characterize the accuracy of clinical suspicion of KS.

Results—A total of 441 patients received 450 biopsies where KS was on the differential diagnosis, and 239 patients (54%) were ultimately diagnosed with KS. The KS cohort was more likely to be male (58% vs. 37%, $P < 0.001$), HIV positive (94% vs. 85%, $P < 0.05$), and have lower CD4 counts at the time of biopsy (274 cells/ μ vs. 362 cells/ μ l, $P < 0.05$). The PPV of clinical suspicion of KS was 58%. When KS was not histopathologically diagnosed, clinically benign diseases were found in 17%, medically significant conditions requiring alternative therapies in 78%, and life-threatening diseases in 5%.

Discussion—Our study reinforces the risk factors in development of KS. The poor PPV supports the important role of histology in KS diagnosis to both ensure appropriate treatment and prevent overtreatment. Improved accessibility to biopsy and augmentation of local dermatopathologic services would likely improve diagnostic accuracy and treatment.

Background

Kaposi's sarcoma (KS) is a vascular malignancy caused by human herpes virus 8 (HHV8) infection that predominantly affects the skin, lymphatics, and gastrointestinal tract in immunocompromised hosts.^{1,2} While antiretroviral therapy (ART) has a substantial impact on KS incidence in resource-rich settings, KS continues to cause significant morbidity and mortality in sub-Saharan Africa (SSA), ranking among the most commonly reported malignancies in this region despite similarly widespread availability of ART.^{3,4} This disparity has been attributed to the scale of the human immunodeficiency virus (HIV) epidemic, delayed access to ART, and higher sero-prevalence of HHV8 in SSA.^{5,6} While management for limited stage disease primarily involves optimizing management of HIV with ART, chemotherapy or radiation are required when disease is more extensive or refractory.^{7–11} These additional therapies carry the potential for serious adverse effects, emphasizing the importance of correct diagnosis and the need for ongoing characterization of the affected population.

The demographics, clinical presentations, and outcomes of adult KS in Botswana are not well characterized. A recent prospective cohort study of 207 patients with KS receiving oncologic treatment in Botswana reported male gender and low CD4 cell count as risk factors.¹² In this cohort, 45% of patients were receiving ART prior to their diagnosis of KS, and a majority of the remaining patients were ART-eligible (CD4 < 250 cells/ μ l).^{12,13} It was proposed that late initiation of ART, particularly in men, and low recognition of early stage KS remained barriers to decreasing disease incidence and progression. Better characterization of the risk factors for KS may allow for earlier and more accurate clinical suspicion of the disease.

In resource-rich settings, the diagnosis of KS is routinely confirmed with histopathology; however, diagnosis in resource-limited settings is challenging due to lack of access to dermatologists, supplies, and the scarce availability of dermatopathology services. In a survey study of SSA nations, 86% of countries reported having histology processing services and a pathologist, but only 14% reported having a dermatopathologist.¹⁴ In addition, long

wait times (>1 month) seem to dissuade use of this diagnostic tool.¹⁴ Without access to reliable histopathology, clinicians must rely heavily on clinical judgment, which can be particularly difficult in immunocompromised patients where presentations can vary widely and the initiation of incorrect empiric therapy can have significant consequences. The concordance of clinical diagnosis of KS with histopathologic diagnosis in countries such as Uganda, Kenya, and South Africa has been reported as positive predictive values (PPV) ranging from 57% to 77%.^{15–17} To date, little is known about the accuracy of clinical diagnosis and the implication of misdiagnoses in Botswana.

We conducted a retrospective review of the cohort of patients biopsied in the dermatology clinic at Princess Marina Hospital (PMH), for whom KS was included in the clinical differential diagnosis, to describe the patient demographics, HIV characteristics, and clinical presentations of these patients. We also evaluated the concordance of clinical suspicion of KS with histopathologic diagnosis to determine the PPV of clinical suspicion of KS in this population.

Materials and methods

Study approval was obtained from the Botswana Ministry of Health and Wellness, the University of Pennsylvania and University of Iowa institutional review boards, and the research committee at PMH.

The dermatology clinic at PMH in Gaborone, Botswana, provides the only specialized dermatologic care in the country. In the case of KS, the dermatology clinic serves as a referral center for patients with suspected disease for further evaluation and consideration of biopsy. The dermatology clinic is primarily staffed by rotating U.S. or Canadian dermatology residents in their final year of training, local dermatology physicians, and occasionally by U.S. attending dermatologists, who decide on the need for biopsy and determine the ultimate clinical differential diagnosis reported to pathologists. Since the clinic's establishment, there has been a gradual shift toward requiring biopsy, particularly for patients being referred to oncology for further treatment. Prior to this, in an effort to balance resource utilization, clinically obvious cases of KS were not always biopsied, and severely ill patients with strongly suspected disease were occasionally referred to oncology prior to biopsy given the delays with histology.

For histopathology, PMH has three general pathologists, one of whom reviews all skin biopsies. When pathology is unclear, the slides are then reviewed virtually by U.S.-trained dermatopathologists with expertise in HIV-related dermatopathology via a robotic microscope.

Data were abstracted from the dermatology clinic's biopsy records and later integrated with data from the Botswana Prospective Cancer Cohort (BPCC) database to obtain additional information on treatment modalities for the subset of patients with KS receiving treatment in the oncology clinic. Initiated in October 2010, the BPCC is currently the largest longitudinal oncology cohort in Botswana, consenting adult (age >18) Botswana citizens with malignancies who were present at the three of the busiest oncology centers in the country –

PMH, Gaborone Private Hospital, and Nyangabgwe Referral Hospital.¹² For this cohort, HIV status and treatment and cancer diagnosis, method of diagnosis, stage, and treatment are obtained on enrollment, and patients are followed prospectively for functional status, treatment response, and survival.

Biopsy logs from the dermatology clinic at PMH dating from September 2008 through June 2015 were reviewed. Clinical records for all patients biopsied for clinically suspected KS, defined as KS being listed on the clinical differential diagnosis, were included for analysis. Patients were excluded if they were not citizens of Botswana or were known to be incarcerated at the time of their evaluation.

Data recorded included demographic information (age, sex), HIV status, HIV characteristics (CD4 counts at the time of biopsy, viral loads, ART regimen, and time on ART at diagnosis), clinical descriptions (lesion morphology and distribution, edema, mucosal involvement, lymph nodes, stool occult blood testing), and histologic descriptions and diagnoses. If two or more biopsies were performed on one patient, each biopsy was considered separately if the corresponding diagnoses were different. If diagnoses of both specimens were identical, the biopsies were aggregated and counted once. For patients also enrolled in the BPCC, treatment regimens (ART regimens $\pm$ chemotherapy or radiation) were recorded.

The demographic and clinical characteristics for the patient population biopsied for suspected KS in the dermatology clinic were analyzed using descriptive statistics. In comparing the characteristics of patients ultimately diagnosed with KS by histology to those who were diagnosed with other skin conditions, chi-square test (Pearson or Fisher's), or Welch's *t* test were used to analyze factors related to HIV status, ART initiation, CD4 cell count, and clinical descriptions at time of biopsy. The PPV of clinical suspicion of KS was defined by the percentage of all biopsies for suspected KS that were definitively interpreted as having KS present. All indeterminate interpretations were excluded from this analysis.

Results

Dermatology cohort

A total of 441 patients had biopsies performed for clinical suspicion of KS in the dermatology clinic at PMH during the study period (Table 1). The average age for this cohort was 40 ± 14 years, and an approximately equal number of men and women were biopsied (217 males and 224 females). HIV status was reported for 403 patients, and 357 (89%) were HIV positive with an average CD4 cell count of 315 ± 219 cells/ μ l at the time of biopsy. Seventy-nine percent of these patients were on ART at the time of biopsy. A majority of the lesions biopsied were described as plaques or nodules involving the upper or lower extremities.

A total of 239 (54%) patients were ultimately diagnosed with KS on histopathology, while alternate diagnoses were made in 188 (43%) patients. A final diagnosis was not available for the remaining 14 (3%) patients either due to insufficient biopsy specimens or unavailable pathology reports.

Characteristics of cases confirmed to be KS

While the age was similar for those diagnosed with KS compared with those with alternative diagnoses (Table 1), a significantly greater proportion of the patients diagnosed with KS were male compared with those diagnosed with other diseases (58% vs. 38%, $P < 0.001$). In addition, significantly more patients diagnosed with KS were HIV positive (94% vs. 85%, $P < 0.05$). The average CD4 cell count at diagnosis was significantly lower in the group diagnosed with KS (274 cells/ μ l vs. 362 cells/ μ l, $P < 0.05$), although there was no difference in percentage of ART coverage at the time of biopsy between the two groups. Newly diagnosed patients with KS who were HIV positive and not yet on ART were referred for therapy. Fourteen patients (6%) diagnosed with KS were found to be HIV negative.

The clinical morphology and distribution did not differ significantly for lesions that were diagnosed as KS by histopathology compared with those with alternative diagnoses, although there was a trend toward significance for involvement of the feet in the KS group ($P = 0.059$).

PPV of clinical suspicion of KS

A total of 450 biopsies were obtained from 441 patients, and a definitive diagnosis was made for 414 specimens. Two hundred and thirty-nine biopsies were ultimately interpreted as KS, which corresponds to a PPV of 58% when there was any mention of KS on the clinical differential diagnosis. Nine patients were biopsied twice, and two were found to have KS on repeat biopsy when the initial biopsies were indeterminate. When KS was not found, a variety of other diagnoses were made (Table 2). Overall, 84% of alternate diagnoses were medically significant in that they merited management that differs from that of KS with 5% of these being acute or life-threatening conditions. The remaining 16% of alternate diagnoses were clinically benign conditions.

Treatment modalities

Most patients with KS are managed with ART. During this study period, the CD4 cell count threshold for ART eligibility increased from 250 cells/ μ l to 350 cells/ μ l in 2012, and individuals with KS or other WHO stage 3 or 4 conditions maintained eligibility for ART, regardless of CD4 cell count.¹³ Data on the specific ART regimens were available for 45 patients, and the most commonly received first-line therapy consisted of tenofovir and emtricitabine in combination with either nevirapine or efavirenz.

For those referred to oncology ($n = 40$), most received additional therapy. Thirty-one patients received chemotherapy (78%), and three of these patients also received radiation (8%). Most patients received low-dose bleomycin, doxorubicin, and vincristine (ABV) every 3 weeks, and one patient received paclitaxel.

Discussion

KS continues to cause a significant disease burden in Botswana despite improved ART coverage in the region. This apparent heterogeneity of KS remains insufficiently understood as does the accuracy of current diagnostic practices for this malignancy. In this study, a

majority of patients diagnosed with KS were male, HIV positive, and had significantly lower CD4 cell counts than those with alternative diagnoses on histopathology, which are consistent with prior studies from countries throughout SSA.^{12,18–22} The average age of our KS cohort was also similar to those reported in the literature (mid to late 30s).^{12,19,20} Endemic KS, KS occurring in absence of HIV infection, accounted for only a limited proportion of cases (6.4%).

Overall, there was a relatively low (58%) PPV for clinical suspicion of KS with a significant number of patients whose histopathology ultimately revealed other significant or life-threatening conditions requiring alternative therapies (84%). Our data suggest that clinical suspicion alone is not always a reliable means for diagnosis given the implications of mistreatment. Our findings were similar to other PPVs reported in recent studies from other countries in SSA, ranging from 57% to 77%.^{15–17} KS is a condition with multiple morphologic variants, and the numerous conditions that can mimic KS clinically contribute to the overall poor PPVs for clinical suspicion of the disease. This underscores the important role of histopathology in definitively diagnosing KS.

Our PPV of clinical suspicion of KS may be lower than anticipated for several reasons. Earlier in the study period, clinical diagnosis was sufficient for referral to oncology so more classic-appearing KS may not have been biopsied. In addition, the dermatology clinic at PMH is a referral center where cases are often of higher acuity and complexity. Our definition of clinical suspicion also included any mention of KS on the clinical differential diagnosis on the pathology requisition without prioritization of the actual clinical suspicion. Given the prevalence of HIV in the patient population served by our dermatology clinic, KS is often included on the differential diagnosis for completeness even in the absence of high clinical suspicion. It is also important to note that the dermatology clinic in Botswana is staffed largely by short-term dermatology resident rotators who have less experience with disease presentations in the local patient population or with diagnosing KS, which may lead to lower accuracy of clinical suspicion of KS compared to other countries with local experienced dermatologists. Sampling error or inaccuracies in histopathology could also alter the PPV.

Given the overall poor PPV of clinical diagnosis of KS, improving accessibility to biopsy would likely improve diagnostic accuracy and treatment, but this can present logistical challenges in resource-limited settings. Pathology is costly and not only are the staff, clinic space, and materials for performing biopsies limited, but the availability of pathologists and the accuracy of histopathologic diagnosis may limit the utility. The quality of tissue processing may be affected and, in many of these settings, histopathologic diagnosis relies on pathologists without expertise in dermatopathology and without access to diagnostic adjuncts such as immunohistochemical stains.¹⁶ Without specific training in dermatopathology, diagnostic accuracy may be lower and result in missed diagnoses of KS. In a prior study, the concordance of African and U.S.-based pathologists for the diagnosis of KS was only 69%.¹⁵ In addition, sent out specimens are commonly lost and results are often considerably delayed.

Our study has several limitations. This is a retrospective review and relies upon data previously entered, which may be incomplete. Data were only available for patients ultimately biopsied for suspected KS, so patients with more classic disease may not be represented, falsely lowering the PPV. Fewer than expected KS positive patients overlapped with the BPCC database. Future studies should aim to follow this population prospectively, monitoring responses to treatment and mortality to further characterize KS patients in Botswana with respect to severity and outcomes.

Our study reinforces the risk factors in development of KS including HIV positivity, male gender, and lower CD4 cell counts. We also found that clinical suspicion of KS alone is not sufficient for diagnosis, and histopathology is imperative for definitive diagnosis to ensure that proper treatment is initiated and to help prevent unnecessary, potentially dangerous overtreatment with chemotherapy or radiation when not indicated. We recognize that there are instances where waiting for histopathologic diagnosis could potentially delay treatment to acutely ill patients. While we emphasize the importance of histopathologic diagnosis, there may be situations where empiric treatment can be life-saving, particularly given the delays in histopathology experienced in low-resource settings. In these situations, clinicians should aim to balance resource utilization with clinical acumen when taking care of patients. Emerging point-of-care and rapid diagnostic tests for KS, should they prove to be sufficient for diagnosis, may have the potential to improve access to accurate diagnosis by overcoming the time and resource burden of histopathology.

Acknowledgments

Funding: Nicholas J. Jackson, MPH MA received support from Clinical and Translational Science Institute grant UL1TR000124UCLA for his work at UCLA statistical core. For the remaining authors none were declared.

Approved by the Institutional Review Board at the University of Pennsylvania and the Botswana Ministry of Health and Wellness.

References

1. Bower M, Dalla Pria A, Coyle C, et al. Prospective stage-stratified approach to AIDS-related Kaposi's sarcoma. *J Clin Oncol* 2014; 32: 409–414. [PubMed: 24378415]
2. Radu O, Pantanowitz L. Kaposi sarcoma. *Arch Pathol Lab Med* 2013; 137: 289–294. [PubMed: 23368874]
3. Casper C The increasing burden of HIV-associated malignancies in resource-limited regions. *Annu Rev Med* 2011; 62: 157–170. [PubMed: 20868276]
4. Semeere AS, Busakhala N, Martin JN. Impact of antiretroviral therapy on the incidence of Kaposi's sarcoma in resource-rich and resource-limited settings. *Curr Opin Oncol* 2012; 24: 522–530.
5. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015; 136: E359–E386. [PubMed: 25220842]
6. Mahy M, Tassie JM, Ghys PD, et al. Estimation of antiretroviral therapy coverage: methodology and trends. *Curr Opin HIV AIDS* 2010; 5: 97–102. [PubMed: 20046154]
7. Chu KM, Mahlangeni G, Swannet S, et al. AIDS-associated Kaposi's sarcoma is linked to advanced disease and high mortality in a primary care HIV programme in South Africa. *J Int AIDS Soc* 2010; 13: 23. [PubMed: 20615222]
8. Gbabe OF, Okwundu CI, Dedicoat M, et al. Treatment of severe or progressive Kaposi's sarcoma in HIV-infected adults. *Cochrane Database Syst Rev* 2014;CD003256.

9. Herce ME, Kalanga N, Wroe EB, et al. Excellent clinical outcomes and retention in care for adults with HIV-associated Kaposi sarcoma treated with systemic chemotherapy and integrated antiretroviral therapy in rural Malawi. *J Int AIDS Soc* 2015; 18: 19929. [PubMed: 26028156]
10. Mosam A, Uldrick TS, Shaik F, et al. An evaluation of the early effects of a combination antiretroviral therapy programme on the management of AIDS-associated Kaposi's sarcoma in KwaZulu-Natal, South Africa. *Int J STD AIDS* 2011; 22: 671–673. [PubMed: 22096054]
11. Network NCC. National Comprehensive Cancer Network Harmonized Guidelines for Sub-Saharan Africa: Kaposi Sarcoma. 2017.
12. Elmore SN, Kayembe MKA, Zola M, et al. Demographic characteristics and preliminary outcomes in a cohort of HIV-positive patients with Kaposi's sarcoma in a high ART coverage setting: a report from Botswana. African Organization for Research in Cancer (AORTIC) Conference Marrakech, Morocco: 2015.
13. Health BMo. 2012 Botswana National HIV & AIDS Treatment Guidelines. 2012.
14. Tsang MW, Kovarik CL. Global access to dermatopathology services: physician survey of availability and needs in sub-Saharan Africa. *J Am Acad Dermatol* 2010; 63: 346–348. [PubMed: 20633808]
15. Amerson E, Woodruff CM, Forrestel A, et al. Accuracy of clinical suspicion and pathologic diagnosis of Kaposi sarcoma in East Africa. *J Acquir Immune Defic Syndr* 2016; 71: 295–301. [PubMed: 26452066]
16. Tsang MW, Kovarik CL. The role of dermatopathology in conjunction with teledermatology in resource-limited settings: lessons from the African Teledermatology Project. *Int J Dermatol* 2011; 50: 150–156. [PubMed: 21244377]
17. van Bogaert LJ. Clinicopathological proficiency in the diagnosis of Kaposi's sarcoma. *ISRN AIDS* 2012; 2012: 565463.
18. Bohlius J, Valeri F, Maskew M, et al. Kaposi's sarcoma in HIV-infected patients in South Africa: multicohort study in the antiretroviral therapy era. *Int J Cancer* 2014; 135: 2644–2652. [PubMed: 24729433]
19. Mohanlal RD, Pather S. Kaposi's sarcoma, a South African perspective: demographic and pathological features. *S Afr Med J* 2015; 105: 375–378. [PubMed: 26242669]
20. Rohner E, Valeri F, Maskew M, et al. Incidence rate of Kaposi sarcoma in HIV-infected patients on antiretroviral therapy in Southern Africa: a prospective multicohort study. *J Acquir Immune Defic Syndr* 2014; 67: 547–554. [PubMed: 25393941]
21. Semeere A, Wenger M, Busakhala N, et al. A prospective ascertainment of cancer incidence in sub-Saharan Africa: the case of Kaposi sarcoma. *Cancer Med* 2016; 5: 914–928. [PubMed: 26823008]
22. Asiimwe F, Moore D, Were W, et al. Clinical outcomes of HIV-infected patients with Kaposi's sarcoma receiving nonnucleoside reverse transcriptase inhibitor-based antiretroviral therapy in Uganda. *HIV Med* 2012; 13: 166–171. [PubMed: 22112164]

Table 1

Demographics and HIV characteristics

Measure	All biopsied patients	KS cohort	Non-KS cohort	KS versus non-KS <i>P</i> value
Age (years) ^a				
Mean ± SD	40 ± 14	40 ± 13	41 ± 14	0.26
Sex ^a				
Male, %	49	58	38	<0.001
Female, %	51	42	62	
HIV status ^b				
Positive, %	89	94	85	0.004
Negative, %	10	6	15	
Specified unknown, %	1			
CD4 counts ^c				
Mean ± SD	315 ± 219	274 ± 201	362 ± 227	0.016
ART status ^d				
Yes, %	79	75	84	0.15
No, %	21	25	16	
Histopathologic diagnosis of KS ^a				
KS cohort, %	54			
Non-KS cohort, %	43			
Unavailable, % ^e	3			

KS, Kaposi's sarcoma; ART, antiretroviral therapy.

Sample sizes for each column:

^a(441, 239, 188);

^b(403, 218, 168);

^c(151, 61, 90);

^d(197, 123, 68).

^e*N* = 11 not reported/processed plus *N* = 3 insufficient specimens and no repeat pathology performed.

Table 2Histopathologic diagnoses made by dermatopathologists when Kaposi's sarcoma was not present ($n = 175$)

Category	N (%)	Diagnosis (n)
Post-traumatic	15 (9)	Scar (4) Keloid (2) Post-inflammatory pigment alteration (5) Foreign body granuloma (1) Pigment incontinence (3)
Vascular tumors or malformations	5 (3)	Angioma (1) Lymphangioma (1) Pyogenic granuloma (2) Nonspecific vascular proliferation (1)
Venous stasis changes	12 (7)	Stasis dermatitis (8) Lipodermatosclerosis (2) Elephantiasis nostras verrucosa (2)
Confirmed or suspected infection	17 (10)	Bacillary angiomatosis (2) Aspergillosis (1) Warts (2) Epidermodysplasia verruciformis (1) Folliculitis (1) Cellulitis (1) Molluscum (2) Nonspecific infection (7)
Eczematous or psoriasiform dermatoses	47 (27)	Psoriasis (5) Eczematous dermatitis (14) Lichen simplex chronicus/Prurigo nodularis (23) Nonspecific dermatitis (5)
Lichenoid/Interface dermatoses	39 (22)	Lichenoid drug eruption (4) Discoid lupus erythematosus (4) Lichen planus (14) Nonspecific lichenoid dermatitis (17)
Benign tumors or cysts	7 (4)	Dermatofibroma (2) Apocrine hydrocystoma (1) Schwannoma (1) Angiofibroma (2) Congenital melanocytic nevus (1)
Other malignant tumors	8 (5)	Squamous cell carcinoma (2) Pigmented squamous cell carcinoma in situ (1) Lymphoma (2) Metastatic adenocarcinoma (1) Melanoma (2)
Other	25 (14)	Confluent and reticulated papillomatosis (1) Sarcoidosis (1) Radionecrosis (1) Normal skin (1) Pigmented purpura (1) Drug-induced photosensitivity (2) "Drug reaction" - unspecified (2) Vasculitis (2) Lichen amyloid (3) Fixed drug eruption (4) Panniculitis (EI/EN) (7)

EI, erythema induratum; EN, erythema nodosum.