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Correspondence to: Hao Feng, MD, MHS, Department of Dermatology, University of Connecticut Health Center, 21 South Rd, 2nd Floor, Farmington, CT 06032

E-mail: haofeng625@gmail.com

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Delayed diagnosis of nonendemic dermatologic diseases: A retrospective review

To the Editor: Despite almost 20% of international travelers reporting a posttravel dermatologic disorder, limited data exist regarding the epidemiology of nonendemic dermatologic diseases (NEDDs) in the United States.[1,2] We sought to

Table I. Demographic and clinical characteristics of cases of NEDDs (n = 78)

Characteristics	Values (n = 78)
Age, y, mean (SD)	40.7 (16.0)
Female sex, n (%)	26 (33.3)
Purpose of travel, n (%)*	
Immigrant	61 (78.2)
US traveler	10 (12.8)
VFR traveler	3 (3.8)
Foreign traveler	1 (1.3)
No travel	3 (3.8)
Region of travel, n (%)†	
Caribbean	21 (26.9)
Sub-Saharan Africa	19 (24.4)
South America	16 (20.5)
Central America	7 (9.0)
South Asia	6 (7.7)
North America	5 (6.4)
Southeast Asia	3 (3.8)
Middle East	2 (2.6)
Oceania	1 (1.3)
Europe	1 (1.3)
Unknown	1 (1.3)
Diagnosis, n (%)	
Hansen disease	27 (34.6)
Lymphatic filariasis	17 (21.8)
Mycetoma	12 (15.4)
Cutaneous leishmaniasis	11 (14.1)
Chromoblastomycosis	5 (6.4)
Onchocerciasis	3 (3.8)
Buruli ulcer	2 (2.6)
Schistosomiasis	1 (1.3)
Dracunculiasis	0 (0.0)
Yaws	0 (0.0)
Exposure, n (%)	
Arthropods	15 (19.2)
Contaminated soil	7 (9.0)
Infected humans	6 (7.7)
Animals	1 (1.3)
Contaminated water	1 (1.3)
Unknown	48 (61.5)
Prior known diagnosis, n (%)	22 (28.2)
Clinical department making new diagnosis, n (%) (n = 56)	
Dermatology	21 (37.5)
Infectious diseases	21 (37.5)
Surgery	4 (7.1)
Primary care	3 (5.4)
Neurology	3 (5.4)
Inpatient	3 (5.4)
Podiatry	1 (1.8)
Time from symptom onset to diagnosis, mo, median (IQR)‡	20 (3.5-72)
Misdiagnosed, n (%)‡	52 (92.9)

IQR, Interquartile range; *NEDD*, nonendemic dermatologic disease; *SD*, standard deviation; *VFR*, visiting friends/relatives.

**Immigrant* indicates a native of another country who has moved to the United States; *US traveler* indicates a native of the United States who has visited another country for less than 6 months; *VFR traveler* indicates a native of another country who has moved to the United States and returns to his/her home country to visit friends or relatives; *foreign traveler* indicates a native of another country who is visiting the United States.

†The total is greater than 100% because some patients traveled to more than 1 region.

‡Of those with a new diagnosis of a NEDD (n = 56).

Table II. NEDDs by purposes of travel (n = 78)

	Purpose of travel,* n (%)				
Diagnosis	**Immigrant (n = 61)**	**US traveler (n = 10)**	**VFR traveler (n = 3)**	**Foreign traveler (n = 1)**	**No travel (n = 3)**
Hansen disease	24 (39.3)	1 (10.0)	2 (66.6)	0 (0.0)	0 (0.0)
Lymphatic filariasis	16 (26.2)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)
Mycetoma	12 (19.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cutaneous leishmaniasis	4 (6.6)	7 (70.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chromoblastomycosis	2 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)
Onchocerciasis	2 (3.3)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)
Buruli ulcer	1 (1.6)	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)
Schistosomiasis	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)

NEDD, Nonendemic dermatologic disease; *VFR*, visiting friends/relatives.
**Immigrant* indicates a native of another country who has moved to the United States; *US traveler* indicates a native of the United States who has visited another country for less than 6 months; *VFR traveler* indicates a native of another country who has moved to the United States and returns to his/her home country to visit friends or relatives; *foreign traveler* indicates a native of another country who is visiting the United States.

characterize the epidemiologic and clinical characteristics of NEDDs, including rates of misdiagnosis and diagnostic delays, across multiple institutions in Boston, Massachusetts.

This retrospective study included adult patients diagnosed with a NEDD between May 25, 1993, and September 30, 2017, at Massachusetts General Hospital, Brigham and Women's Hospital, and Faulkner Hospital. Patients were identified by International Classification of Diseases (ICD), Ninth and 10th Revision, codes using the Research Patient Data Registry—a large institutional clinical data warehouse—and confirmed by review of each patient's clinical, laboratory, and pathologic data. Patients with inaccurate ICD codes or inadequate data to confirm diagnoses were excluded. NEDDs included for evaluation represented nonendemic skin neglected tropical diseases (Table I).[3] Patient-level data reviewed included demographics, travel purpose, travel region, documented exposures, clinical department of diagnosis, time from symptom onset to diagnosis, and history of prior misdiagnosis.

A total of 78 cases of NEDDs were identified. Demographic and clinical characteristics are summarized in Table I. The majority of cases were seen in immigrants (n = 61, 78.2%), whereas US travelers (n = 10, 12.8%), travelers visiting friends and relatives in their native country (n = 3, 3.8%), foreign travelers (n = 1, 1.3%), and patients with no travel (n = 3, 3.8%) composed the minority of cases. The most frequently visited regions were the Caribbean (n = 21, 26.9%), Sub-Saharan Africa (n = 19, 24.4%), and South America (n = 16, 20.5%).

Among NEDDs, the most frequent diagnosis was Hansen disease (n = 27, 34.6%), followed by lymphatic filariasis (n = 17, 21.8%), mycetoma (n = 12, 15.4%), and cutaneous leishmaniasis (n = 11, 14.1%). The most common disease in immigrants was Hansen disease (n = 24, 39.3%), whereas the majority (n = 7, 70.0%) of US travelers had cutaneous leishmaniasis (Table II). Of the 56 new NEDD diagnoses, most were diagnosed by dermatologists (n = 21, 37.5%) or infectious diseases physicians (n = 21, 37.5%). Of the new diagnoses, 92.9% (n = 52) had been misdiagnosed previously, and the median time from symptom onset to diagnosis was 20 months (IQR, 3.5-72).

Although rare in the United States, NEDDs are seen, particularly in immigrant populations. In our study, the majority of cases were misdiagnosed by a health care provider, leading to a median diagnostic delay of 20 months. Diagnostic delays may be due to patient (eg, late presentation to health care providers), clinician (eg, underrecognition of NEDDs), or systems (eg, lack of insurance among immigrants) factors and can contribute to substantial disease-associated morbidity. For example, delays in the diagnosis of Hansen disease lead to irreversible nerve damage and disability in endemic regions.[4,5]

Limitations include the study's retrospective design and a lack of confirmatory pathology or serology in some cases. Additionally, reliance on ICD codes likely underestimates true case counts because of inaccurate coding. Thus, our results do not reflect true disease prevalence. Despite these limitations, our study shows that the diagnoses of NEDDs are frequently delayed in the United States. Clinicians should especially consider NEDDs in immigrants or recent travelers with cutaneous findings that are not typical for an endemic diagnosis.

Cristina Thomas, MD, and Vinod E. Nambudiri, MD, MBA

From the Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

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Correspondence to: Vinod Nambudiri, MD, MBA, Brigham and Women's Hospital, Department of Dermatology, 221 Longwood Ave, Boston, MA 02115

E-mail: vnambudiri@bwh.harvard.edu

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Low recurrence rates for challenging squamous cell carcinomas using Mohs micrographic surgery with AE1/AE3 cytokeratin immunostaining

To the Editor: Local recurrence rates of high-risk cutaneous squamous cell carcinoma (SCC) are lower after Mohs micrographic surgery compared with conventional excision.[1] Although local recurrence rates of primary cutaneous SCC after Mohs micrographic surgery are low,[1,2] local recurrence can reach 15% or higher for tumors with high-risk factors.[3] Adjuvant AE1/AE3 cytokeratin immunohistochemical stains ease visualization of SCC in challenging cases by helping to identify single-cell spread, neoplastic cells masked by inflammation, and perineural invasion.[4] We conducted a retrospective study of SCC cases treated with Mohs micrographic surgery with immunohistochemical stain and present 5-year Kaplan-Meier local recurrence rates.

Table I. Patient and tumor clinical characteristics

Characteristics	n (%)
No. of patients	288
No. of tumors	348
Sex	
Women	86 (24.7)
Men	262 (75.3)
Age at surgery, y	
Mean (range)	70.8 (28.8-100.2)
Race	
Black	10 (2.9)
Asian	3 (0.9)
White	316 (90.8)
Hispanic Latino	3 (0.9)
Other	7 (2.0)
Unknown	9 (2.6)
Immunosuppression status	
Immunosuppressed*	90 (25.9)
BWH staging system	
T1 (0 risk factors)†	80 (23.0)
T2a (1 risk factor)	166 (47.7)
T2b (2−3 risk factors)	92 (26.4)
T3 (≥4 risk factors or bone invasion)	10 (2.9)
Tumor anatomic location	
Head/neck	210 (60.3)
Ear	32 (9.2)
Lips	21 (6.0)
Trunk	14 (4.0)
Extremities	39 (11.2)
Hands/feet	28 (8.0)
Genitalia	4 (1.1)
Tumor histology	
Good differentiation	41 (11.8)
Moderate differentiation	52 (14.9)
Poor differentiation	54 (15.5)
In situ	25 (7.2)
Unknown	176 (50.6)
Tumor characteristics	
Perineural invasion ≥0.1 mm	39 (11.2)
Mean length (range), cm	3.0 (0.2-12.1)
Mean width (range), cm	2.6 (0.1-12.7)
Mean no. of stages (range)	1.41 (1-6)
Most recent follow-up, y	
Mean (range)	3.55 (0.02-9.2)
Median	3.15

Data are presented as No. (%) unless otherwise indicated.
BWH, Brigham and Women's Hospital.
*Patients were considered immunosuppressed if they had solid organ transplant, chronic lymphocytic leukemia, or rheumatoid arthritis, or were receiving an immunosuppressant medication.
†Brigham and Women's Hospital risk factors include preoperative tumor diameter greater than or equal to 2 cm, poorly differentiated histology, perineural invasion greater than or equal to 0.1 mm, and tumor invasion beyond subcutaneous fat.