

willing to provide follow-up care for uninsured screening participants with suspicious lesions identified at screening events. Centralized follow-up tracking protocols and transportation incentives<sup>5</sup> may also enhance access to follow-up care.

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Funding sources: None.

Conflicts of interest: None disclosed.

Reprints not available from the authors.

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<https://doi.org/10.1016/j.jaad.2018.12.011>

### Eosinophilic dermatosis of hematologic malignancy: A retrospective cohort of 37 patients from an Italian center



To the Editor: Eosinophilic dermatosis of hematologic malignancy (EDHM) is a nonspecific skin disease that is primarily associated with chronic lymphocytic leukemia.<sup>1-3</sup> Despite being a common disease in the hematology setting, often misdiagnosed as an

“exaggerated reaction to mosquito bites,”<sup>2</sup> there is a shortage of dermatology-oriented reports. We report on a retrospective case series of EDHM carried out in our department between November 2014 and January 2017. The main results are listed in Table I.

We identified 37 patients on the basis of the proposed EDHM diagnosis criteria, which include: 1) a known history of oncohematologic disease; 2) recurrent episodes of papules, nodules, urticarial plaques, or blisters with intense pruritus; 3) eosinophilic infiltration upon histopathology; and 4) the exclusion of other causes of tissue eosinophilia.<sup>1</sup> The majority suffered from indolent B cell disorders, primarily B cell chronic lymphocytic leukemia (51%) and various types of B cell non-Hodgkin lymphomas (30%), whereas acute leukemia was observed in 4 patients (10%). At the time of EDHM onset, only a minority of them (25%) underwent chemotherapy because of active/progressive disease.

The eruption was widespread, albeit mostly occurring on the lower limbs (90%) and upper limbs (79%). However, more than half of the cases had lesions on the trunk, and 25% of patients reported painful lesions on the face, scalp, and neck.

Most of the patients presented with pruritic erythematous papules, plaques, and nodules with a smooth surface and color ranging from slightly pink to bright red, or more cyanotic hues. In one third of cases, tense blisters resembling bullous pemphigoid (BP) were evident, especially on the legs (Fig 1, A).

Skin specimens revealed variably dense, mainly perivascular lymphohistiocytic and eosinophilic infiltrates in the papillary and mid-dermis in most cases (80%), extending to the reticular dermis and subcutaneous fat in 20% of cases. In 2 cases, the histologic features resembled those of Wells syndrome, revealing numerous eosinophils with flame figures in the reticular dermis. Dermoepidermal detachment was observed in 10 cases, raising the suspicion of BP. In these cases, direct immunofluorescence was negative. No relevant epidermal changes were found, except for spongiosis in 2 specimens (Fig 1, B).

Almost all patients showed some clinical benefit with the proposed treatment; most patients were treated with systemic steroids either with or without concomitant topical steroids. A minority of patients achieved clinical improvement with other regimens, including doxycycline with or without nicotinamide and ultraviolet A1 light phototherapy. The overall response rate was 93%. However, in many cases (63%) the response was short-lived, and the patients relapsed.

Our study shows that EDHM potentially occurs in a wide range of hematologic cancers, with

**Table I.** Summary of the main results of the study, including demographic, clinical, and therapeutic data in patients with eosinophilic dermatosis of hematologic malignancy

Characteristic	Value
Enrolled patients, N	37
Male, n (%)	17 (46)
Female, n (%)	20 (54)
Associated malignancies, n (%)	
B cell chronic lymphocytic leukemia	19 (51)
B cell non-Hodgkin lymphoma	11 (30)
Multiple myeloma/monoclonal gammopathy of undermined significance	2 (5)
Acute leukemia	4 (10)
Aggressive T-cell lymphoma	1 (2.5)
Mean age at time of hematologic diagnosis, y (median [range])	66 (67 [40-88])
Mean age at time of EDHM diagnosis, y (median [range])	70 (74 [41-89])
Mean latency between hematologic diagnosis and EDHM, months (median [range])	57 (40 [5-191])
Mean follow-up, months (median [range])	8.7 (5 [0-34])
Previous exposure to chemotherapy, n/N (%)	27/34 (80)
On chemotherapy at time of skin rash, n/N (%)	7/34 (20)
Mean duration of rash, months (median [range])	7 (3.5 [1-34])
Seasonality, n/N (%)	
Spring	13/37 (35)
Summer	10/37 (27)
Autumn	9/37 (24)
Winter	5/37 (13)
Involved sites, n/N (%)	
Head/neck	9/37 (24)
Trunk	20/37 (54)
Upper limbs	30/37 (81)
Lower limbs	34/37 (91)
Type of lesions, n/N (%)	
Papules	28/37 (75)
Plaques	17/37 (45)
Nodules	15/37 (40)
Vesicles	7/37 (19)
Blisters	12/37 (32)
Therapy, n/N (%)	
Prednisolone 0.5 mg/kg/day	16/34 (46)
Prednisolone 1.0 mg/kg/day	8/34 (23)
Topical steroids	12/34 (35)
Oral antihistamines	6/34 (18)
Cyclosporine	1/34 (3)
Ultraviolet A1 light phototherapy	2/34 (6)
Doxycycline	4/34 (12)
Oral nicotinamide 1 g/day	4/34 (12)
Overall response rate, n/N (%)	28/30 (93)

Continued

**Table I.** Cont'd

Characteristic	Value
Complete responses	12/30 (40)
Partial responses	16/30 (53)
No response	2/30 (7)
Relapse rate, n/N (%)	12/19 (63)
Mean relapse-free interval, months (median [range])	5 (4 [1-14])
On chemotherapy at time of relapse, n/N (%)	3/12 (25)

EDHM, Eosinophilic dermatosis of hematologic malignancy.

differing biologic behavior and of either lymphoid or myeloid origin. Because of its clinicopathologic heterogeneity and its tendency to persist over long periods, it may represent both a diagnostic and therapeutic challenge. The overlap with BP should be kept in mind to avoid misdiagnosis and may have led to an overestimation of the BP incidence in this setting.<sup>1,4,5</sup> Aside from systemic steroids, doxycycline, nicotinamide, and ultraviolet A1 light phototherapy could be effective therapeutic alternatives considering their lower long-term toxicity, but these data warrant further prospective investigations.

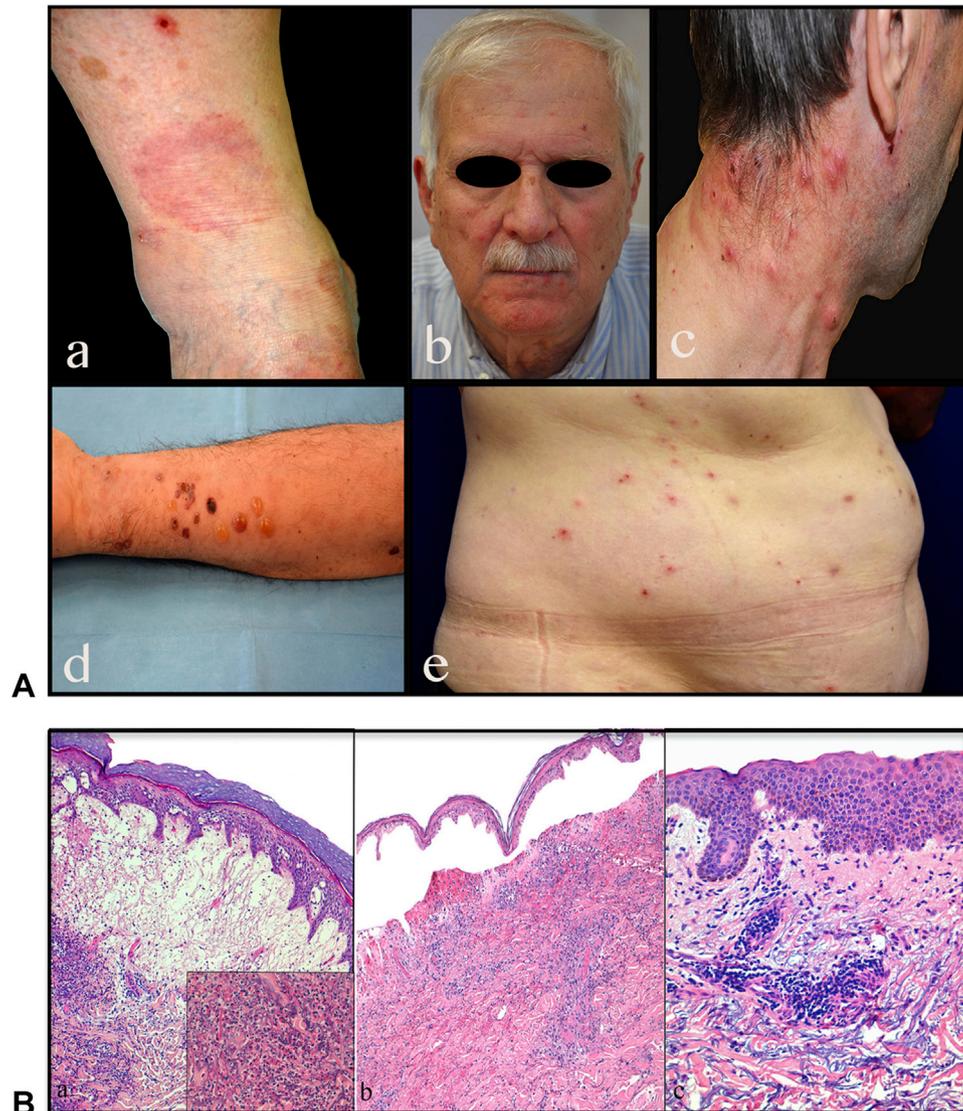
In conclusion, we believe that EDHM is an underestimated disorder. Although there is no evidence to suggest that EDHM has a negative impact on the prognosis for the underlying malignancy, it has significant negative implications for patients given its uncomfortable symptoms and chronic, relapsing course. The main limitation of this study is its retrospective design. Further pathophysiological insights and long-term prospective studies are advisable to gain a better understanding of this disorder and to optimize patient management.

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Funding sources: None.

Conflicts of interest: None disclosed.



**Fig 1. A,** Distinct clinical presentations of eosinophilic dermatosis of hematologic malignancy. **(a)** Light pink plaque on a leg resembling Wells syndrome. **(b)** and **(c)** Multiple erythematous papules and nodules on the head and neck. **(d)** Tense blisters, some hemorrhagic, on the forearm. **(e)** Multiple monomorphic, centered erythematous papules on the trunk that persisted for months. **B,** Distinct histopathologic presentation of eosinophilic dermatosis of hematologic malignancy. **(a)** Extensive intra- and subepidermal edema with dermoepidermal detachment and an intense, perivascular, mixed inflammatory infiltrate with numerous eosinophils, extending from the papillary into the reticular dermis, resembling Wells syndrome. At higher magnification, it becomes possible to observe flame figures, consisting of hypereosinophilic collagen fibers surrounded by degranulated eosinophil granulocytes. **(b)** Dermoepidermal unilocular detachment. Mixed-type inflammatory infiltrate with a few superficial perivascular and dermal eosinophilic granulocytes. **(c)** Acanthosis and mild epidermal spongiosis. Edema of the papillary dermis. Presence of a moderate, inflammatory interstitial infiltrate consisting of eosinophilic granulocytes in the papillary and mid-dermis. **(B [a-c],** Hematoxylin–eosin stain; original magnification: **[a** and **c]**,  $\times 10$ ; **[a, inset]**,  $\times 40$ ; **[b]**,  $\times 20$ .)

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<https://doi.org/10.1016/j.jaad.2018.11.048>

**Rhinophyma is associated with alcohol intake**



*To The Editor:* Rhinophyma has been considered a sign of excessive drinking since antiquity despite a lack of quality data. We therefore conducted a case-control study at Strasbourg Hospital, with private practice dermatologists, to evaluate this association.

We included 52 cases of prevalent rhinophyma between December 2015 and July 2017 and compared each with 3 age- and sex-matched dermatologic controls without facial dermatoses (N = 156)

by using standardized questionnaires to evaluate alcohol intake (units/wk), severity of rhinophyma on the National Rosacea Society scale (0-3), and other factors (Table I). Statistical analyses were conducted by using a mixed-effects logistic regression model.

The male-to-female sex ratio was 25:1, and the median age was 69 years (range, 47-91). Rhinophyma was associated with erythema and telangiectasia (94.2%), papulopustules (46.2%), and other types of phymas (19.2%). The median alcohol intake was 14 units/wk [range, 3-24] in cases versus 3 units/wk [range, 0-8.5] in controls. Alcohol intake was low (0-7 units/wk) in 40.4% of cases, moderate (8-21 units/wk) in 32.7%, and excessive (>21 units/wk) in 26.9%. The risk of rhinophyma was high for moderate drinkers (odds ratio [OR], 4.14; 95% confidence interval [CI], 1.41-12.15; *P* = .010) and higher in excessive drinkers (OR, 17.33; 95% CI, 3.96-75.1; *P* < .001). Applying the Poisson model (Fig 1) revealed a significant correlation between alcohol intake and severity of rhinophyma. Multivariate analysis showed a strong association with family history of rhinophyma (OR, 160.7; 95% CI, 27.3-944.6) and diabetes (OR, 6.45; 95% CI, 2.29-18.2), but not with other parameters (Table I).

The role of alcohol in rosacea has long been debated, but studies addressing rhinophyma directly are rare and controversial.<sup>1-4</sup> The only such study was retrospective, showing that of the 45 individuals with rhinophyma, 22% were excessive drinkers versus 8% of the 45 controls, with no difference in

**Table I.** Complementary clinical data: Univariate and multivariate analysis

Associations	Cases	Controls	Univariate analysis OR P value		Multivariate analysis OR P value	
Median BMI	28.7 kg/m <sup>2</sup>	26.8 kg/m <sup>2</sup>	<b>1.10</b>	<b>.003</b>	1.06	.268
Family history of rhinophyma	46% (n = 23)	1.3% (n = 2)	<b>65.6</b>	<b>&lt;.001</b>	<b>160.7</b>	<b>&lt;.001</b>
Phototype						
I	0	4.5% (n = 7)	Reference		Reference	
II	38.5% (n = 20)	35.3% (n = 55)				
III	51.9% (n = 27)	40.4% (n = 63)				
IV	9.6% (n = 5)	19.2% (n = 30)	0.43	.098	0.60	.45
VI	0	0.6% (n = 1)				
VI	0	0				
Professional sun exposure	34.6% (n = 18)	41.7% (n = 65)	0.74	.369		
Smoking						
None	28.8% (n = 15)	49.4% (n = 77)	Reference		Reference	
Active	53.8% (n = 28)	35.3% (n = 55)	1.92	.174	0.83	.816
Past	17.3% (n = 9)	15.4% (n = 24)	<b>2.61</b>	<b>.009</b>	1.67	.337
Liver disease						
Chronic	3.9% (n = 2)	6.4% (n = 10)	0.58	.497		
Alcoholic	3.9% (n = 2)	1.3% (n = 2)				
Type 2 diabetes mellitus	42.3% (n = 22)	16.7% (n = 26)	<b>3.67</b>	<b>&lt;.001</b>	<b>6.45</b>	<b>&lt;.001</b>
Dyslipidemia	48.1% (n = 25)	35.3% (n = 55)	1.70	.102	2.03	.150
Hypertension	65.4 (n = 34)	48.7% (n = 76)	<b>1.99</b>	<b>.039</b>	1.17	.758

Bold indicates statistically significant results.  
BMI, Body mass index; OR, odds ratio.