Qing Yu Weng, BS,[a] Elizabeth Buzney, MD,[a] Cara Joyce, PhD,[b] and Arash Mostaghimi, MD, MPA, MPH[a]

Department of Dermatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA[a]; Department of Biostatistics, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA[b]

QYW and EB contributed equally.

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Correspondence to: Arash Mostaghimi, MD, MPA, MPH, Department of Dermatology, Department of Medicine, Brigham & Women's Hospital, Harvard Medical School, 15 Francis St, PBB-B 421, Boston, MA 02115

E-mail: amostaghimi@bwh.harvard.edu

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Supplemental Table I. Distribution of non-adherent patients by number of phototherapy treatments attended

# Treatments	N (%) of early non-adherent
0	103 (67.3)
1	15 (9.8)
2	7 (4.6)
3	7 (4.6)
4	9 (5.9)
5	5 (3.3)
6	7 (4.6)

Clinicopathological and dermoscopic features of angio-eccrine hyperplasia in clear cell acanthoma

To the Editor: While the histological epidermal criteria (psoriasiform acanthosis, pale-appearing keratinocytes, parakeratosis, and neutrophilic exocytosis) of clear cell acanthoma (CCA) are usually well known,[1] the dermal ones have been less investigated. We attempted to evaluate the frequency of vascular and eccrine findings in CCA and to correlate them with dermoscopy (Fig 1 and Supplemental Fig 1 [available at http://www.jaad.org]).

Histological specimens of CCA removed in the last 8 years have been reviewed. For each sample, we evaluated gender, age, anatomical site (lower limbs or other anatomical sites), presence of angio-eccrine hyperplasia (AEH), and vascular hyperplasia of the papillary dermis (VHPD).We defined as VHPD the usual presence of a vascular hyperplasia in the papillary dermis; while as AEH, the presence of a hyperplastic vascular component associated with an increase of the eccrine glands and hyperplasia of the sweat glands, in the medium and deeper dermis. In order to evaluate a possible exogenous role on the pathogenesis of VHPD and AEH, we tested *Human Herpes virus 8* (HHV8) expression, through an immunohistochemical essay. For a statistical reprocessing of data, we used the Fisher exact test between AEH and the single variables.

A total of 20 specimens of CCA from 12 men (60%) and 8 women (40%) were collected (Table I). Median age of the cohort was 67.5 years (range, 37-77 years). Fifteen specimens (75%) were referred to lesions removed on the lower limbs, 4 (20%) on the trunk, and 1 (5%) on the upper limbs. In 16 (80%) specimens, we found AEH in the dermis. Among those, 11 (55%) cases showed also a VHPD. Notably, in 4 (20%) cases, both AEH and VHPD were absent. Dermoscopic images were available for 15 cases, including the 4 cases without AEH and VHPD (Table I). For these latter 4 cases, dermoscopy revealed unusual features including irregular arranged hairpin, dotted, and glomerular (coiled) vessels (Fig 2). In contrast, the remaining cases revealed the typical "string of pearls" vascular pattern (Fig 1). None of the analysed specimens showed positivity to HHV8. We found a significant association between AEH and VHPD ($P = .02$) and between AEH and dermoscopy ($P = .001$), while for the other variables the statistical significance was not reached. Furthermore, no significant correlation was found for histologic and dermoscopic findings, according to the anatomical site.

AEH is a frequent and repetitive dermal clue in CCA (Supplemental Fig 2; available at http://www.jaad.org).

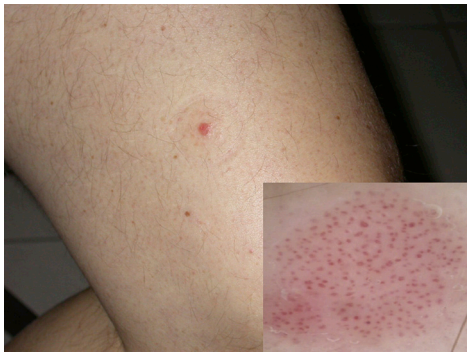

Fig 1. Clinical and dermoscopy (inset) of a clear cell acanthoma located on the lower limb. Dermoscopy reveals a typical "string of pearls" vascular pattern.

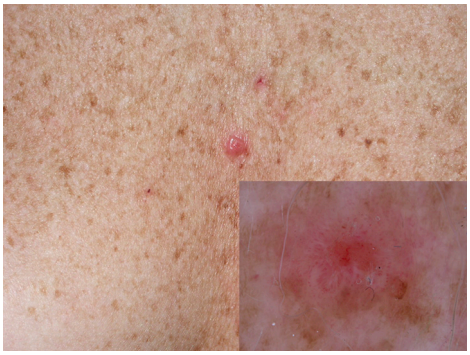

Fig 2. Clinical of a clear cell acanthoma (CCA) of the trunk. Dermoscopy (inset) shows linear and irregular hairpin vessels (flower-like) and globular/dotted vessels. The lesion was in the differential diagnosis with amelanotic melanoma. Histologically, there was an absence of angio-eccrine hyperplasia (AEH) and vascular hyperplasia of the papillary dermis (VHPD).

Table I. Clinic-pathological and dermoscopical baselines of clear cell acanthoma (CCA)

Patient N°	Age	Gender	Site	VHPD	AEH	Dermoscopy
1	77	F	LL	—	—	AP
2	69	M	LL	—	Yes	NP
3	76	M	LL	—	Yes	PLD
4	75	M	LL	Yes	Yes	PLD
5	48	F	LL	Yes	Yes	PLD
6	45	F	Trunk	—	—	AP
7	70	M	LL	Yes	Yes	PLD
8	48	F	LL	—	Yes	PLD
9	37	M	UL	—	Yes	NP
10	37	M	LL	—	Yes	PLD
11	60	F	LL	Yes	Yes	PLD
12	57	M	LL	—	—	AP
13	60	F	LL	Yes	Yes	PLD
14	62	M	LL	Yes	Yes	PLD
15	68	M	LL	—	—	AP
16	73	F	LL	Yes	Yes	PLD
17	67	F	LL	Yes	Yes	NP
18	70	M	Trunk	Yes	Yes	NP
19	70	M	Trunk	Yes	Yes	NP
20	70	M	Trunk	Yes	Yes	PLD

AEH, Angio-eccrine hyperplasia; *AP*, atypical pattern; *LL*, lower limbs; *N*, patient's number; *PLD*, typical pinpoint-like/dotted vessels with a pearl—necklace-like distribution; *NP*, not provided; *UL*, upper limbs; *VHPD*, vascular hyperplasia of the papillary dermis.

The absence of AEH/VHPD is associated with an unspecific dermoscopy, without creating the typical dotted and coiled vessels arranged in a linear and reticular distribution (Supplemental Fig 3; available at http://www.jaad.org).[2] In fact, these latter are directly related to AEH, which explains the linear and organized distribution of vessels, as well as with VHPD, which corresponds to the capillaries oriented perpendicular within the elongated dermal papillae.

The presence of AEH/VHPD increases the dermoscopic sensitivity and specificity of CCA, reducing pitfalls with thick hypomelanotic/amelanotic melanomas, other pink tumors, and inflammatory lesions, as psoriasis where the vessels occupy the whole lesion.[2-4]

The pathogenesis of CCA remains unknown, and the absence of HHV8 excludes its probable role in the angiogenesis of AEH/VHPD. Maybe the higher incidence of CCA in lower limbs of elderly patients favors a reactive nature, probably induced by a stasis dermatitis.

Giovanni Paolino, MD,[b] Pietro Donati, MD,[a] Angela Ferrari, MD,[a] Chiara Panetta, MD,[a] Pierluigi Buccini, MD,[a] Michele Donati, MD,[a] and Iris Zalaudek, MD[c]

Dermatopathological Laboratory, San Gallicano Institute of Rome,[a] Clinica Dermatologica, La Sapienza University of Rome,[b] Rome, Italy; Dermatology Department, Medical Univeristy of Graz, Graz, Austria[c]

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Correspondence to: Giovanni Paolino, MD, Clinica Dermatologica, La Sapienza University of Rome, Viale del Policlinico 15, 00186 Rome, Italy

E-mail: gio8519@libero.it

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Lack of evidence that bedbugs transmit pathogens to humans

To the Editor: The global population of bedbugs that feed on humans (*Cimex lectularius, Cimex hemipterus,* and *Leptocimex boueti*) has undergone a significant resurgence since the late 1990s. Due to increased international travel and pesticide resistance, bedbugs once thought to be native to certain geographic locations have been found in other parts of the world. Bedbugs present a socioeconomic burden because they are costly to eradicate and infestations often recur. According to the US Environmental Protection Agency, bedbugs are "a pest of significant health importance," and upwards of 45 disease pathogens have been reported in bedbugs.[1,2] It stands to reason to ask if bedbugs might transmit human pathogens.

We performed a literature review on August 6, 2015, and searched the computerized medical bibliographic databases PubMed, EMBASE, CINAHL, and Web of Science with the search terms: "bedbug" OR "cimex lectularius." A total of 1790 articles were returned, and 12 articles were suitable for inclusion (clinical and laboratory published studies [1990 to 2015] investigating bedbugs as potential vectors of infectious disease) after screening of titles, abstracts, and/or full-text articles. These articles demonstrated that although bedbugs may carry pathogens such as methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus faecium*, and hepatitis B virus, and may be competent vectors of *Bartonella quintana* and *Trypanosoma cruzi*, there were no confirmed cases of human disease transmission.

Previous reports suggest that, although a number of different disease pathogen species have been detected in or on bedbugs, there is a lack of definitive evidence that bedbugs transmit human pathogens.[1,3] An important challenge for scientists is to determine the reason for this interesting finding.

One hypothesis relates to the fact that bedbugs are the only hematophagous arthropod that both feeds on humans and mates by traumatic insemination. Traumatic insemination results in the repeated introduction of pathogens and repeated immune stimulation in the female bedbug, and may thereby select for higher levels of immunity in bedbugs. As a result, the survival and viability of pathogens maintained within bedbugs may be affected.[1] Another hypothesis is that bedbug saliva has been reported to contain lysozymes and other peptides that may have antimicrobial activities.[4,5]

Future research related to these or other hypotheses might lead to greater scientific understanding of how to limit pathogen transmission in humans, and be of significant benefit for patients and global health by preventing human transmission of a variety of infectious diseases.

Derek Ho, BS,[a] Olivia Lai, BS,[b] Sharon Glick, MD,[c] and Jared Jagdeo, MD, MS[a,c,d]

Dermatology Service, Sacramento VA Medical Center, Mather, CA[a]; Keck School of Medicine of University of Southern California, Los Angeles, CA[b]; Department of Dermatology, State University of New York Downstate Medical Center, Brooklyn, NY[c]; Department of Dermatology, University of California Davis, Sacramento, CA[d]

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Correspondence to: Jared Jagdeo, MD, MS, Sacramento VA Medical Center, Building 801 — Dermatology Service, 10535 Hospital Way, Mather, CA 95655

E-mail: jrjagdeo@gmail.com

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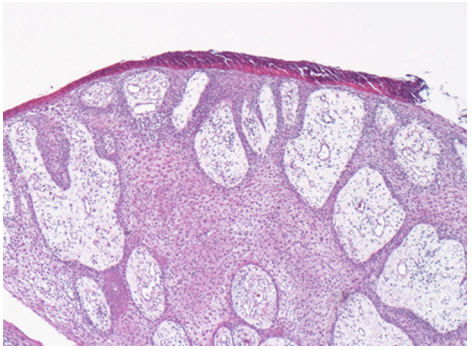
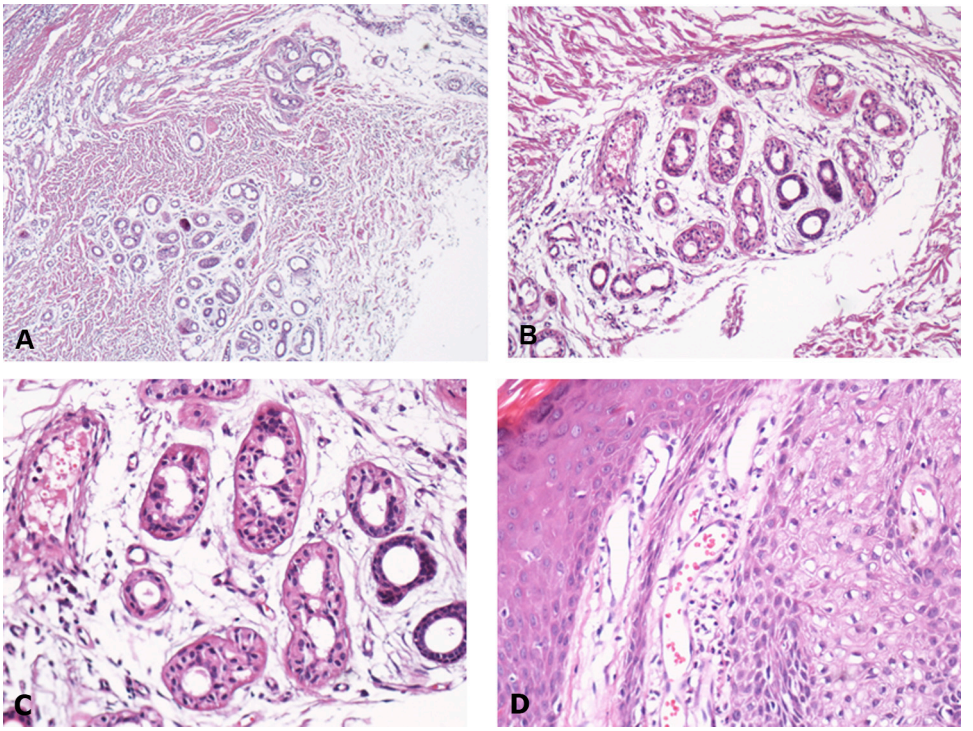
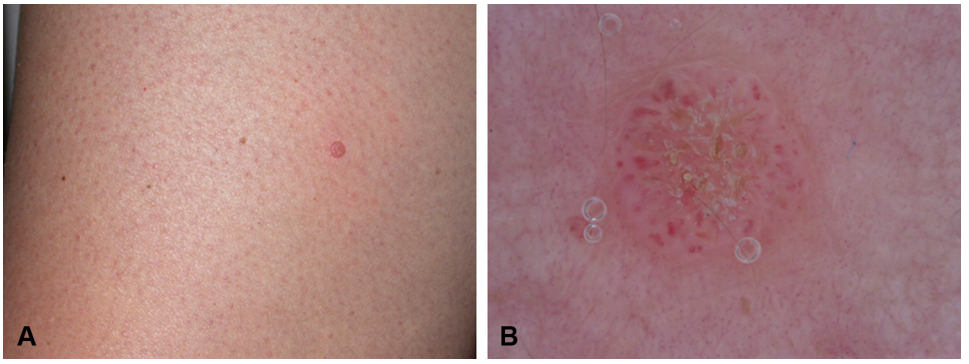


Supplemental Fig 1. Histological features of a clear cell acanthoma, with a vascular hyperplasia of the papillary dermis (VHPD). (Hematoxylin and eosin stain; original magnification: ×10)



Supplemental Fig 2. A-B, Angio-eccrine hyperplasia (AEH) at level of the dermis; (Hematoxylin and eosin, 10× and 20×); **C**, A particular of the AEH. (Hematoxylin and eosin, 40×); **D**, A particular of a usual vascular hyperplasia of the papillary dermis (VHPD). (Hematoxylin and eosin; original magnification: ×40)



Supplemental Fig 3. A, Clinical image of another CCA with atypical dermoscopic features; **B**, Dermoscopy shows hairpin vessels with a central area of hyperkeratosis. The lesion was in the differential diagnosis with keratoacanthoma and seborrheic keratosis. Histologically. there was an absence of angio-eccrine hyperplasica (AEH) and vascular hyperplasia of the papillary dermis (VHPD).