Pruritic blisters on legs and feet

Was recent outdoor fieldwork to blame for the pruritic blisters on this US Navy sailor's feet and calves?

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A 23-year-old active duty US Navy sailor came to our medical center for treatment of 1–2 cm tense pruritic blisters on his dorsal feet, calves, and anterior lower extremities **(FIGURE 1).** He told us that several days earlier, he had noticed ill-defined "itchy red bumps" on both legs. He denied fever, night sweats, malaise, trauma, insect bites, contact with animals or plants, or recent illnesses. He did say, however, that he'd recently done outdoor fieldwork with the Marine Corps in southern California.

His medical history was unremarkable, and he was not taking any prescribed or over-the-counter medications or supplements. He had no family history of blistering or other autoimmune disorders.

On examination, we noticed clear fluid-filled vesicles and bullae on non-erythematous, non-urticarial bases that were haphazardly distributed on both legs and dorsal feet. Agminated or herpetiform configurations were not present. Ruptured bullae left erythematous to beefy red eroded bases, and there were numerous smaller red papules with vesicular surface changes. All of the lesions were below the knees; there was complete sparing of the trunk, upper extremities, intertriginous skin, head, and neck.

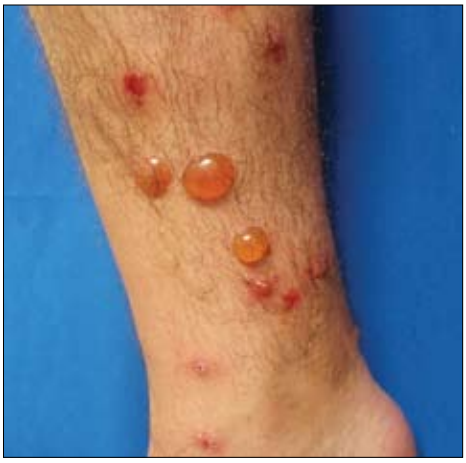
The remainder of the physical examination was unremarkable, and there was no lymphadenopathy. Complete blood count and chemistries were within normal limits, and the patient's HIV status was negative.

We performed lesional and perilesional punch biopsies. The lesional biopsy demonstrated subepidermal blistering with a predominantly eosinophilic infiltrate in all layers of the dermis and within the blister. Direct immunofluorescence (DIF) was performed on the perilesional biopsy and was negative for IgA, IgG, IgM, C3, and fibrinogen. Gram stain, potassium hydroxide (KOH) prep, and wound culture were also negative.

What is your diagnosis?

FIGURE 1

Tense pruritic blisters



A 23-year-old active duty US Navy sailor sought treatment for non-erythematous pruritic blisters on his lower legs and dorsal feet. He had no lesions on his trunk, upper extremities, intertriginous skin, head, or neck.

PHOTO BY WILFRED LUMBANG, MD

FAST TRACK

All of the patient's lesions were below the knees

FAST TRACK

The distribution of lesions and the lack of systemic illness are sufficient for diagnosis

Diagnosis:

Bullous arthropod bite reaction

Bullous arthropod bite reaction (BABR) occurs in sensitized individuals as a delayed hypersensitivity immune reaction to insect saliva.[1] Patients typically present with grouped localized pruritic or asymptomatic blistering[2] and otherwise appear well. Unless secondarily infected, the blisters are non-erythematous and non-purulent, and develop within hours to days of the bite.

Lesion location is key. The distribution and location of the lesions will tip you off to a BABR diagnosis. The lesions in BABR are usually grouped and localized to a specific area of the body, depending on the causative arthropod and the circumstances leading to the bites. For example:

- **Lesions caused by *Cheyletiella* mites** are typically found on the forearms, anterior thighs, and lower abdomen after an infested pet sits on an individual's lap.[2,3]
- **Blisters caused by flea bites** are isolated to the lower extremities.[4] (We suspect that flea bites were the culprit in our patient's case.)
- **Lesions caused by *Cimex lectularius,*** more commonly known as bedbugs, may be found on the entire body and tend to occur in groups of 3.[5]

Insect bite? What insect bite?

Most patients will only complain of pruritus and will tell you that they don't recall having had any insect bites.[6] That said, the distribution of the lesions, lack of systemic illness, and otherwise unremarkable physical exam are sufficient for diagnosis.

Occasionally, a punch biopsy with DIF may be necessary to rule out more serious bullous disorders. In BABR, you may see both subepidermal and intraepidermal blistering, with perivascular and interstitial eosinophilic and lymphocytic infiltrates. Blisters separated by strands of keratinocytes create a characteristic multilocular appearance. Unlike autoimmune blistering disorders, DIF is negative in BABR.[7] Gram stain, Tzanck smear, bacterial culture, and KOH prep may also provide additional information if infection is a concern.

For certain patients, the DX may be less clear-cut

Similar bullous lesions following insect bites have been reported in patients with HIV,[8] chronic lymphocytic leukemia,[9–12] EBV-associated Natural Killer leukemia/lymphoma,[13] and mantle cell lymphoma.[14] There is ongoing debate as to whether the vesicular lesions in these patients truly represent an exaggerated response to an arthropod bite or mimic an insect-like bite reaction.[10,12]

Nevertheless, when you suspect a patient has BABR, be aware of its association with both hematologic malignancies and HIV. Appropriate evaluation, such as HIV screening and complete blood count, should be performed.

A condition that mimics contact dermatitis

Clinically and histologically, BABR can mimic the following:

- **Contact dermatitis.** With contact dermatitis, the blistering is more likely to appear in streaks or in a linear fashion.[15] Lesions will be painful, as well as pruritic, and occur following direct contact with a plant or chemical allergen.
- **Drug-induced pemphigoid.** The patient's history will increase your suspicion of drug-induced pemphigoid. Patients may be taking sulfur-containing drugs (furosemide), antibiotics (penicillins, fluoroquinolones), antihypertensives (ACE inhibitors, calcium channel blockers), neuroleptics, or sulfasalazine.[7,16,17] The eruption is usually more generalized than BABR, and may involve the mucous membranes.
- **Fungal infections.** These infections will typically occur on the palms and

soles. Infiltrate is typically neutrophilic, but can be eosinophilic.[18]

- **Bullous scabies.** Patients will have severe pruritus. Burrows and lesions can typically be found on moist areas (periumbilical, intertriginous skin).[19,20]
- **Bullous pemphigoid.** This is more commonly seen in elderly patients with comorbid conditions. Onset of blistering is gradual, and occurs predominantly on flexural skin.

Pemphigoid gestationis, erythema toxicum neonatorum, incontinentia pigmenti, and some pemphigus variants also have predominantly eosinophilic infiltration in the skin. These, however, are clinically distinct from BABR.

Focus on symptoms and prevention

BABR will resolve over time without aggressive intervention. Most patients are treated symptomatically with oral antihistamines and topical steroids for pruritus.[1] Prevention of further bites is important because of the risk of arthropod-transmitted diseases.[21]

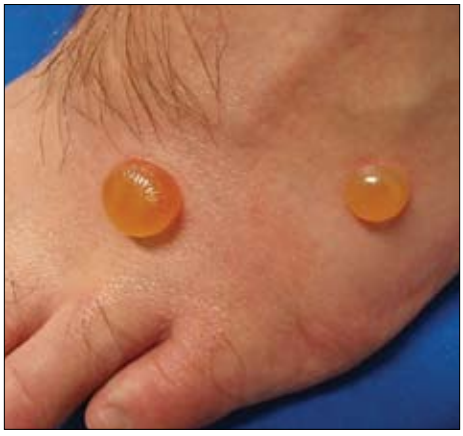
Our patient couldn't comfortably wear shoes

Our patient had extensive tense blistering on both legs that prevented him from comfortably wearing shoes **(FIGURE 2)**. Using a #11 blade, we punctured all of the blisters at the most dependent portion of each lesion. We decompressed the lesions, but did not de-roof them so that the blistered skin could serve as a biological dressing. We applied topical mupirocin and wrapped both legs with a compressive dressing.

We gave the patient a 2-week tapering course of oral prednisone. At the 3-week follow-up, all of the blistered skin had completely healed with the exception of post-inflammatory hyperpigmentation. No new lesions developed. Our patient was well, with no recurrence of blistering, at his 6-month follow-up. ■

FIGURE 2

Wearing shoes was a problem



Our patient's extensive tense blistering precluded him from comfortably wearing shoes. We punctured and decompressed the lesions, but did not de-roof them. The blistered skin served as a biological dressing.

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Disclosure

The authors reported no potential conflict of interest relevant to this article. The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States government.

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FAST TRACK

Treatment centers on oral antihistamines and topical steroids for pruritus

THE JOURNAL OF
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Evidence-based medicine ratings

THE JOURNAL OF FAMILY PRACTICE uses a simplified rating system called the Strength of Recommendation Taxonomy (SORT). More detailed information can be found in the February 2003 issue, "Simplifying the language of patient care," pages 111–120.

Strength of Recommendation (SOR) ratings are given for key recommendations for readers. SORs should be based on the highest-quality evidence available.

- **A** Recommendation based on consistent and good-quality patient–oriented evidence.
- **B** Recommendation based on inconsistent or limited-quality patient-oriented evidence.
- **C** Recommendation based on consensus, usual practice, opinion, disease-oriented evidence, or case series for studies of diagnosis, treatment, prevention, or screening

Levels of evidence determine whether a study measuring patient-oriented outcomes is of good or limited quality, and whether the results are consistent or inconsistent between studies.

STUDY QUALITY

1—Good-quality, patient-oriented evidence (eg, validated clinical decision rules, systematic reviews and meta-analyses of randomized controlled trials [RCTs] with consistent results, high-quality RCTs, or diagnostic cohort studies)

2—Lower-quality patient-oriented evidence (eg, unvalidated clinical decision rules, lower-quality clinical trials, retrospective cohort studies, case control studies, case series)

3—Other evidence (eg, consensus guidelines, usual practice, opinion, case series for studies of diagnosis, treatment, prevention, or screening)

Consistency across studies

Consistent—Most studies found similar or at least coherent conclusions (coherence means that differences are explainable); *or* if high-quality and up-to-date systematic reviews or meta-analyses exist, they support the recommendation.

Inconsistent—Considerable variation among study findings and lack of coherence; *or* if high-quality and up-to-date systematic reviews or meta-analyses exist, they do not find consistent evidence in favor of the recommendation.

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