

Richard P. Usatine, MD, Feature Editor

Rupturing bullae not responding to antibiotics

John Sauret, MD

Department of Family Medicine, State University of New York at Buffalo

A 33-year-old African American woman came to the office with a 2-week history of skin lesions and itching. The lesions started with a single blister on her left elbow; numerous other blisters subsequently appeared on her forearm and hands. One week before this visit, she had been given a presumptive diagnosis of bullous impetigo and was treated with cephalexin.

Despite the antibiotics, other lesions soon appeared in the nuchal and breast folds, axillae, and scalp areas. Several had ruptured, producing purulent, malodorous material. She had no known allergies, no medical problems aside from obesity, and no significant family history or recent travels. She denied any illicit drug use and had not been on any medications.

FIGURE 1 Bulla on the index finger



Left index finger bulla, which appeared 10 days after onset of disease.

On physical exam, 1 large bulla was seen on the fourth digit of her left hand (**Figure 1**). The patient was obese, and inspection of the skin folds of her abdomen showed multiple suppurative lesions and erosions where previous bullae were found (**Figure 2**). No oral or gingival erosions were seen.

Labs showed a white blood cell (WBC) count of 10.5×10^9 L], hemoglobin of 11.0 g/dL, and hemoglobin A_{1c} of 5.5; liver function tests were normal. Gram stain showed no WBC and had rare Gram-positive bacilli. Potassium hydroxide prep of a skin lesion scraping showed no fungal elements. A herpes culture was performed along with a punch biopsy.

■ WHAT IS THE DIAGNOSIS?

FIGURE 2 Multiple bullae on the trunk



Right breast and abdominal folds with multiple flaccid bullae and denuded areas.

■ DIFFERENTIAL DIAGNOSIS

Many diseases manifest with bullae/vesicles. Workup should begin with a complete history and physical exam. A skin biopsy may be needed to make a definitive diagnosis.

Herpes zoster typically manifests with clustered pruritic vesicular lesions on a red base that follow a dermatomal distribution. *Pemphigus vulgaris* appears with flaccid blisters, erosions, and tend to have oral mucosal lesions. A positive Nikolsky's sign is characteristic of pemphigus vulgaris. *Bullous impetigo* appears with scattered lesions of erythema and macules, progressing to thin roofed bullae and subsequently to "honey-crusted" lesions. In *toxic epidermal necrolysis*, the bullae are widespread and lead to sloughing of the skin. *Pyoderma gangrenosum* has ulcer formation preceded by pustules that typically expand rapidly to approximately 20 cm. These ulcers have necrotic bluish edges.

Diagnostic test results

The patient's herpes culture was negative. Fortunately, the punch biopsy was sent for direct immunofluorescence. Direct immunofluorescence showed positive staining with immunoglobulin (Ig) G in the intercellular regions of the epidermis and no staining with IgA, IgM, C3, or fibrinogen. Hematoxylin and eosin-stained sections showed suprabasal blistering containing neutrophils and a few eosinophils. These results are consistent with pemphigus vulgaris.

■ DIAGNOSIS: PEMPHIGUS VULGARIS

Pemphigus vulgaris is blistering disease involving the skin and mucous membranes, with severe morbidity and occasional mortality. Prior to the development of effective treatment, the disease was 75% fatal within 5 years.¹

Its prevalence is equal among men and women, with a rate of occurrence of 0.5/100,000 people per

year. The average age of onset is in the fifth and sixth decades of life, but there is wide variation in age. It has multiple causes and risk factors (Table).

The clinical manifestation of pemphigus typically features mucocutaneous blisters followed by erosions. Often they appear first in mucous membranes and may not appear cutaneously until several months later.² The skin lesions are painful flaccid blisters that may appear anywhere. A characteristic finding of pemphigus vulgaris is the Nikolsky sign, in which lateral stress applied to perilesional skin causes an expansion of the blistering.

There are 2 major subtypes of pemphigus. *Pemphigus vulgaris* has blisters extending to the deep epidermis, and *pemphigus foliaceus* has more superficial involvement of the epidermis. Pemphigus can also be seen in paraneoplastic syndromes.

In pemphigus, the epidermal cells lose normal cell contacts and form a blister. Electron microscopy shows desmosomal abnormalities at desmosomal junctions. It is these junctions that guarantee the integrity of the epithelium. Direct immunofluorescence shows IgG deposition in intercellular spaces.

■ TREATMENT: STEROIDS AND ADJUVANT DRUGS

Inducing remission is the main goal of therapy for pemphigus vulgaris. Epidemiological studies have shown up to a 75% remission rate 10 years after initial diagnosis.³ Corticosteroids are the preferred therapy for the management of pemphigus vulgaris (based on expert opinion). Also, adjuvant drugs such as azathioprine and cyclophosphamide are commonly used in combination with corticosteroids, with the aim of increasing efficacy and of having a steroid-sparing action (level of evidence: 5, expert opinion).

A tailored dosing schedule of steroids has been advocated according to the severity of the disease. Mild disease can be treated with an initial prednisone dose of 40 to 60 mg/d; in severe cases, 60 to 100 mg/d. Other agents that have been used to treat pemphigus vulgaris are intramuscular gold, dapsone, and intravenous immunoglobulin.

Correspondence: John Sauret, MD, Department of Family Medicine, State University of New York at Buffalo, 150 Family Medical Modular Complex, Buffalo, NY 14214-3013. E-mail: sauret@buffalo.edu.

TABLE

Causes and risk factors for pemphigus vulgaris

Penicillamine
Captopril
Rifampin
Phenol-based drugs
Amide-based drugs
Foods: garlic, leek, onion
Pregnancy
Pesticide exposure
Herpes virus infection
Cytomegalovirus infection
Epstein-Barr virus infection

Adapted from: Benner et al 2003.⁴

■ PATIENT OUTCOME

The patient was treated with oral prednisone starting at 60 mg/d and her skin began to clear. A full course of oral prednisone was continued and tapered over 1 month. Currently, she remains in remission off all medications.

■ CONCLUSION

Pemphigus vulgaris is a potentially life-threatening condition that must be recognized and treated promptly. With a lack of large-scale controlled studies, the diagnosis and management of pemphigus vulgaris has based on expert opinion.³

The blisters appear first in mucous membranes and may not appear cutaneously for several months

Complications such as superimposed infection of the lesions, cellulitis, and sepsis can occur. Its association with underlying neoplasm, thymomas, myasthenia gravis, and other autoimmune disorders warrants consideration for additional workup when indicated.

REFERENCES

1. Sami N, Ahmed AR. Dual diagnosis of pemphigus and pemphigoid. Retrospective review of 30 cases in the literature. *Dermatol* 2001; 202:293–301.
2. Ahmed AR, Graham J. Pemphigus: current concepts. *Ann Intern Med* 1980; 92:396–405.
3. Harman KE, Albert S, Black MM. Guidelines for the management of pemphigus vulgaris. *Br J Dermatol* 2003; 149:926–937.
4. Benner S, Mashiah J, Tamir E, Goldberg I, Wohl Y. PEMPHIGUS: an acronym for a disease with multiple etiologies. *Skinmed* 2003; 2:163–167.

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