ONLINE EXCLUSIVE

THE PATIENT

57-year-old man

SIGNS & SYMPTOMS

– Type 2 diabetes
– Neuropathy
– Bilateral foot blisters

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The authors reported no potential conflict of interest relevant to this article.

doi: 10.12788/jfp.0472

THE CASE

A 57-year-old man with type 2 diabetes, hyperlipidemia, and obesity presented to the emergency department (ED) for bilateral foot blisters, both of which appeared 1 day prior to evaluation. The patient's history also included right-side Charcot foot diagnosed 4 years earlier and right foot osteomyelitis diagnosed 2 years prior. He had ongoing neuropathy in both feet but denied any significant pain.

The patient wore orthotics daily and he'd had new orthotics made 6 months prior; however, a recent COVID-19 diagnosis and prolonged hospital stay resulted in a 30-pound weight loss and decreased swelling in his ankles. He acquired new shoes 2 weeks prior to ED presentation.

Physical examination revealed large blisters along the medial aspect of the patient's feet, with both hemorrhagic and serous fluid-filled bullae. The lesions were flaccid but intact, without drainage or surrounding erythema, warmth, or tenderness. The blister on the left foot measured 8 x 5 cm and extended from the great toe to mid-arch (**FIGURE**), while the one on the right foot measured 8 x 3 cm and extended from the great toe to the base of the proximal arch. Sensation was decreased in the bilateral first and second digits but unchanged from prior documented exams. Bilateral dorsalis pedis pulses were normal.

Work-up included imaging and lab work. The patient's complete blood count was normal, as were his erythrocyte sedimentation rate and C-reactive protein level. Radiographs of the right foot were normal, but those of the left foot were concerning, although inconclusive, for osteomyelitis. Further evaluation with magnetic resonance imaging of his left foot revealed a deformity of the first digit with some subchondral signal change that was thought to be posttraumatic or degenerative, but unlikely osteomyelitis.

FIGURE

Flaccid but intact hemorrhagic bullae on left foot

IMAGE COURTESY OF VIDANT MEDICAL CENTER, GREENVILLE, NC

THE DIAGNOSIS

Podiatry was consulted for blister management. Based on atraumatic history, rapid appearance, location of blisters, unremarkable lab work and imaging, and concurrent diabetes, the patient received a diagnosis of bilateral bullous diabeticorum (BD).

CONTINUED

DISCUSSION

Roughly one-third of patients with diabetes will experience some cutaneous adverse effect because of the disease.[1] Common iterations include acanthosis nigricans, rash, or even infection.[2] BD is a rare bullous skin lesion that occurs in patients with diabetes; it has a reported annual incidence of 0.16% and may be underdiagnosed.[1]

Cases of BD have been described both in patients with longstanding diabetes and in those newly diagnosed, although the former group is more often affected.[1] BD is reported more frequently in males than females, at a ratio of 2:1.[1,3] Patients ages 17 to 80 years (average age, 55 years) have received a diagnosis of BD.[1] Most affected patients will have a concomitant peripheral neuropathy and sometimes nephropathy or retinopathy.[1]

The etiology of BD is unclear but appears to be multifactorial. Hypotheses suggest that there's a link to neuropathy/nephropathy, excessive exposure to ultraviolet light, or a vascular cause secondary to hyaline deposition in the capillary walls.[4,5]

Although A1C values do not correlate with blister formation, patients with hypoglycemic episodes and highly varying blood glucose values seem to have higher rates of bullous diabeticorum occurrence.

What you'll see at presentation

The typical manifestation of BD is the rapid appearance of tense blisters, which may occur overnight or even within hours.[1] They are usually painless; common locations include the feet, distal legs, hands, and forearms.[1,5] The bullae can be serous or hemorrhagic.[1]

Most notable in the patient's history will be a lack of trauma or injury to the area.[1] Although A1C values do not correlate with blister formation, patients with hypoglycemic episodes and highly varying blood glucose values seem to have higher rates of occurrence.[1]

Other sources of blistering must be ruled out

The diagnosis of BD is clinical and based on history, exam, and exclusion of other bullous diagnoses.[6] A key clue in the history is the spontaneous and rapid onset without associated trauma in a patient with diabetes.[6] Direct immunofluorescence, although nonspecific, can be helpful to rule out other disorders (such as porphyria cutanea tarda and bullous pemphigoid) if the history and exam are inconclusive. Direct and indirect immunofluorescence is typically negative in BD.[4,6]

The differential diagnosis includes other conditions that involve bullae—such as frictional bullae, bullous pemphigoid, and bullous systemic lupus erythematosus—as well as porphyria, erythema multiforme, insect bites, or even fixed drug eruption.[2,7]

- **Porphyria** tends to develop on the hands, whereas BD most commonly occurs on the feet.[5]
- **Erythema multiforme** typically includes inflammatory skin changes.[5]
- **Trauma or fixed drug eruption** as a cause of blistering lesions would be revealed during history taking.

Considerations for treatment and follow-up

Without treatment, blisters often self-resolve in 2 to 6 weeks, but there is high likelihood of recurrence.[6,8] There is no consensus on treatment, although a typical course of action is to deroof the blister and examine the area to rule out infection.[6] The wound is then covered with wet-to-dry gauze that is changed regularly. If there is suspicion for or signs of underlying infection, such as an ulcer or skin necrosis, antibiotics should be included in the treatment plan.[7]

- **Additional considerations.** Patients will often need therapeutic footwear if the blisters are located on the feet. Given the higher prevalence of microvascular complications in patients with diabetes who develop BD, routine ophthalmologic examination and renal function testing to monitor for microalbuminuria are recommended.[5]
- **Our patient** underwent bedside incision and drainage and was discharged home with appropriate wound care and follow-up.

THE TAKEAWAY

BD cases may be underdiagnosed in clinical practice, perhaps due to patients not seeking help for a seemingly nonthreatening condition or lack of clinician recognition that bullae are related to a patient's diabetes status. Prompt recognition and proper wound care are important to prevent poor outcomes,

such as ulceration or necrosis. JFP

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