Bullous Pemphigoid: Clinical Aspects and Treatments

Ryan S. Q. Geng, MSc and R. Gary Sibbald, MD, MEd, FRCPC, MACP, MAPWCA, JM

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GENERAL PURPOSE: To review the risk factors and clinical features of bullous pemphigoid (BP) and discuss available treatment options.

TARGET AUDIENCE: This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and registered nurses with an interest in skin and wound care.

LEARNING OBJECTIVES/OUTCOMES: After participating in this educational activity, the participant will: 1. Summarize the clinical features and manifestations associated with BP. 2. Identify evidence-based methods to diagnose BP. 3. Explain evidence-based pharmacologic management strategies for the effective treatment of BP.

ABSTRACT: Bullous pemphigoid (BP) is the most common subepidermal blistering disease. It is typically observed in the older adult population and rarely in children. Classic BP is characterized by tense blisters filled with clear or hemorrhagic fluid on normal skin or erythematous base with predilection for flexor surfaces. The criterion standard for diagnosing BP is with direct immunofluorescence for detection of linear deposition of immunoglobulin G or C3 at the dermoepidermal junction and/or indirect immunofluorescence for immunoglobulin G at the basement membrane zone. Treatments with efficacy in treating BP rely on anti-inflammatory or immunosuppressive properties, with corticosteroids being the primary choice of treatment. This review focuses on the clinical presentation, epidemiology, risk factors, and treatment options for BP.

Keywords: anti-inflammatory therapy, autoimmune disease, bullous pemphigoid, differential diagnoses, immunosuppressive therapy, subepidermal blistering disease

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INTRODUCTION

Bullous pemphigoid (BP) is the most common type of subepidermal blistering disease, but it is an uncommon disease overall, with incidence varying between 2.4 and 21.7 new cases per million population.[1] Although BP can be observed in all age groups, it is most prevalent in the older adult population, with a mean age at presentation between 66 and 83 years, which is atypical for an autoimmune disease.[1]

Ryan S. Q. Geng, MSc, is Medical Student, Temerty School of Medicine, University of Toronto, Toronto, Ontario, Canada. R. Gary Sibbald, MD, MEd, FRCPC, MACP, MAPWCA, JM, is Professor of Medicine and Public Health, Dalla Lana School of Public Health & Division of Dermatology, Department of Medicine, University of Toronto.

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The pathogenesis of BP is unclear but is likely multifactorial with an underlying autoimmune etiology. The main pathogenesis pathways involve loss of self-tolerance in B and T cells due to an imbalance between autoreactive helper T cells and regulatory T cells and activation of Toll-like receptors. The result is the production of immunoglobulin (Ig) G or IgE autoantibodies that are characteristic of BP. The autoantibodies are directed against the cytoskeletal linker protein, bullous pemphigoid antigen 1 (BP230), and collagen XVII, bullous pemphigoid antigen 2 (BP180), with BP180 being the main autoantigen.[2] Binding of the autoantibodies to their targets results in complement activation; recruitment of mast cells, neutrophils and eosinophils; and release of proinflammatory cytokines and degradative matrix metalloproteases. The subsequent breakdown of hemidesmosome structures, degradation of extracellular matrix, and inflammatory infiltrate are believed to cause the blister formation observed in BP.[3]

Bullous pemphigoid blisters are intensely pruritic and can impair a patient's ability to perform their activities of daily living. Given the physical and emotional toll that BP places on patients, it is unsurprising that many BP patients experience psychosocial distress, including depression, negative body image, and social isolation.[4] Further, BP is associated with several comorbidities including multiple sclerosis, diabetes mellitus, and psoriasis.[5] There is especially strong association with dementia and cerebrovascular disease, likely related to the expression of BP180 and BP230a in the central nervous system and BP230b in the myocardium.[5,6] In this review, the authors describe the risk factors and clinical features of BP and discuss available treatment options.

Triggers and risk factors

Although the pathogenesis of BP remains unclear, several factors have been identified that predispose individuals to developing BP or to trigger flares of BP (Table 1). Predisposing risk factors include genetic polymorphisms and aging-related immunosenescence. Genetic polymorphisms in the human leukocyte antigen (HLA) class II alleles have been associated with the development of BP, with the HLA-DQB1*03:01 allele having particularly strong evidence for association with BP. Other implicated genes include mitochondrial ATPase synthase 8, P-glycoprotein, and cytochrome P450 2D6.[7]

The development of BP is frequently associated with the use of systemic therapies. However, because older adult patients are often on multiple systemic therapies and BP primarily affects older adults, it is difficult to study the relationship between specific drug use and BP onset. Nonetheless, several classes of medications have been implicated in triggering BP, with the most commonly implicated drugs including dipeptidyl peptidase 4 inhibitors, immune checkpoint inhibitors, loop diuretics, and penicillin and its derivatives (Table 1).[8] The pathogenesis of drug-induced BP is unclear, but theories include interactions between drugs with similar structures and the immune system to trigger an immune response, drugs acting as antigens while covalently bound to endogenous proteins, drug interactions with endogenous proteins leading to exposure of hidden antigenic sites, and inactivation of immunoregulatory processes of T cells. Other potential trigger factors include irritant or allergic contact hypersensitivity reaction to topicals, infection, radiotherapy, burns, and phototherapy.[9]

TABLE 1. PREDISPOSING AND TRIGGER FACTORS FOR BULLOUS PEMPHIGOID

Predisposing Risk Factors	Trigger Factors
Aging-related immunosenescence	Allergic/irritant contact hypersensitivity reactions
Genetic polymorphisms	Burns
HLA class II	Drug classes
MT-ATP8	Angiotensin-converting enzyme inhibitors
ABCB1	Antibiotics (eg, penicillin/derivatives)
CYP2D6	β-Blockers
	Calcium-channel blockers
	Dipeptidyl peptidase 4 inhibitors
	Diuretics
	Immune checkpoint inhibitors
	Nonsteroidal anti-inflammatory drugs
	Salicylates
	Tumor necrosis factor α inhibitors
	Infection
	Phototherapy
	Radiotherapy

Abbreviations: ABCB1, P-glycoprotein; CYP-2D6, cytochrome P450 CYP-2D6; HLA, human leukocyte antigen; MT-ATP8, mitochondrial ATPase synthase 8.

Clinical features and differential diagnoses

The clinical presentation of BP is heterogeneous but is characterized by the appearance of large tense blisters. In the prodromal phase of classic BP, patients may experience intense pruritus alone or in conjunction with the appearance of papular or urticarial lesions. This presentation later evolves into the bullous phase within weeks to months, where vesicles and bullae begin to appear.[10] Blisters can arise on normal skin or on an erythematous base and are usually filled with clear fluid, but may also be hemorrhagic. These blisters can appear anywhere on the body but mostly commonly develop on flexor regions, including the lower abdomen, axilla, upper thighs, and flexor forearms. Prevalence estimates for mucosal involvement in BP range between 5.7% and 18.6%, with the oral mucosa being most common.[11] Mucosal involvement is associated with more extensive cutaneous disease, and patients may require more aggressive therapy to achieve remission.[12] Blisters are present for several days before resolving as erosions and crusts.[10] Postinflammatory hyperpigmentation is typically present after the blisters heal, but without scarring or milia formation. Although recurrences and flares can occur, BP is typically self-limited, and most patients achieve remission within 5 years.[13]

The criterion standard for diagnosing BP is through the detection of linear deposition of IgG or C3 at the dermoepidermal junction by direct immunofluorescence (IIF), with the sample ideally being taken from normal-appearing perilesional skin. Immune deposits in lesional skin may be partially or completely degraded, resulting in a higher risk of false negatives.[14] A lesional skin biopsy at the edge of a blister should also be taken for histopathology studies, where a subepidermal split with superficial perivascular inflammatory infiltrate and eosinophils is supportive of a diagnosis of BP.[10] Indirect IIF for anti-basement membrane zone antibodies and enzyme-linked immunosorbent assay (ELISA) for anti-BP180 autoantibodies can also be performed.[14] Although ELISA can also be performed for anti-BP230 autoantibodies, the specificity is lower compared with anti-BP180.[15] For anti-BP180 autoantibodies, ELISA is preferred over IIF for tracking disease activity because BP180 is the main autoantigen implicated in BP pathogenesis and IIF primarily detects reactivity to BP230.[16]

Clinical presentations of BP are shown in Figure 1. Less common forms of BP are discussed below. Due to the polymorphic presentation of BP, a wide range of differential diagnoses should be considered. Table 2 summarizes differential diagnoses of BP and distinguishing features.

Childhood BP

Bullous pemphigoid occurring in children is very rare and primarily occurs in children older than 8 years. In childhood BP, there is more frequent involvement of mucosal membranes, and in children younger than 1 year, there is more frequent involvement of hands and feet. Childhood BP is benign and self-limited, and remission is achieved rapidly.[17]

Dyshidrosiform BP

In dyshidrosiform BP, the blistering lesions mainly occur on the palms and soles. However, lesions may also subsequently or concurrently appear in other parts of the body as well.[18]

Erythrodermic BP

In erythrodermic BP, patients present with erythroderma (widespread erythema covering most of the body due to inflammation of the skin) along with blister formation.[19]

Localized BP

Localized BP affects only a specific region of the body, rather than being more widespread. Localized BP is infrequent, but has been reported following trauma, radiotherapy, phototherapy, and burns. Localized BP rarely evolves into the more generalized classic BP and responds well to local treatment with topical or intralesional corticosteroids.[20]

Nodular BP

In nodular BP, patients typically present with pruritic, hyperkeratotic, and excoriated nodules on their extremities that are then followed by blistering within weeks to months.[21] This form of BP is similar to prurigo nodularis, except that prurigo nodularis does not present with blisters or have IIF or immunoserologic evidence of BP (Table 2).

Urticarial BP

In urticarial BP, intensely pruritic urticarial wheals are the sole presenting lesion and are not responsive to systemic antihistamines.[22]

Vegetative BP

In the vegetative form of BP, lesions are characterized as purulent and vegetative (bacteria surrounded by a layer of platelets and fibrin) plaques observed in intertriginous regions (skin folds) including the axillae, groin, and thighs.[23] This form of BP exhibits clinical resemblance to pemphigus vegetans. However, in pemphigus vegetans, the blisters observed are flaccid, there is a positive Nikolsky sign, and patients typically present with stomatitis (Table 2).

Vesicular BP

In the vesicular form of BP, the primary lesions are vesicles rather than the larger tense blisters. Patients with the vesicular form of BP present with multiple small, tense vesicles distributed symmetrically as opposed to the random distribution of blisters observed in classic BP.[24] This form of BP resembles dermatitis herpetiformis; however, the severity of presentation of dermatitis

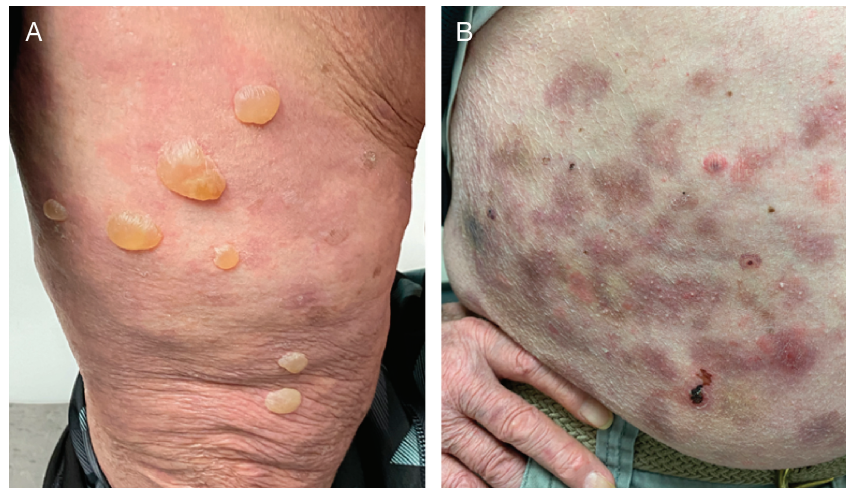

FIGURE 1. CLINICAL PRESENTATIONS OF BULLOUS PEMPHIGOID (BP)
A, Tense clear blisters on an erythematous base localized on the anterior right thigh. B, Excoriations and postinflammatory hyperpigmentation from resolved BP blisters localized on the abdomen. Note the new erythematous early blisters on the medial abdomen. Patients provided permission for their images to be published.

herpetiformis correlates with gluten ingestion, and the lesions have a predilection for extensor surfaces (Table 2).

TREATMENT OF BP

Although BP is a self-limited disease, it is important to provide an early diagnosis and initiate appropriate treatment; mortality associated with BP can be high because BP primarily affects patients with poorer overall health and advanced age. Treatments with anti-inflammatory or immunosuppressive properties are effective in treating BP. The goals of therapy are to control the skin eruptions, prevent recurrence, control itch, and improve quality of life. Treatment choice should be made with consideration of patient age, comorbidities, and use of concurrent medications. A review of current medications should also be conducted to rule out drug-induced BP. Table 3 summarizes the treatment options for BP.

Topical treatments

Corticosteroids

The first-line option is clobetasol propionate 0.05% cream, a superpotent corticosteroid. It is recommended to be administered once or twice daily over the entire body, sparing the face, until adequate disease control is achieved (the preexisting lesions begin to heal, pruritic symptoms cease, and no new lesions form). For mild to moderate disease, 20 to 30 g/d should be applied, whereas 30 to 40 g/d should be applied for extensive disease. Progressive tapering should then be undertaken over a period of 4 to 12 months.[25]

In one trial, 312 patients with either moderate or extensive BP were treated with either a milder 10 to 30 g/d regimen for 4 months or a standard 30 to 40 g/d regimen for 12 months. Bullous pemphigoid was controlled in 98% of patients on the milder regimen compared with 100% in the standard regimen, demonstrating noninferiority of the milder regimen to the standard regimen.[26] Although topical clobetasol propionate is effective in treating BP, it is expensive and requires continuous nursing to aid in application in areas difficult to reach by the patient. Clinical expertise may necessitate the use of other corticosteroids in patients with relative contraindications to superpotent corticosteroids (eg, clobetasol). These relative contraindications may include easy bruising with high-dose oral corticosteroid therapy, skin fragility from other reasons, and lesions located on the face or body folds.

Tacrolimus

Tacrolimus is a calcineurin inhibitor that has demonstrated efficacy as an adjuvant therapy in BP. However, larger trials assessing efficacy are lacking, and available evidence is limited to case reports and series. In a case series involving two patients, adequate control was not achieved with prednisone 60 mg/d, mycophenolate mofetil 1.5 g/d, doxycycline 200 mg/d, and niacinamide 1 g/d or with prednisone 20 mg/d, tetracycline 2 g/d, and niacinamide 2 g/d. However, the addition of topical tacrolimus twice daily resulted in clearing of BP lesions in 2 weeks and allowed for tapering of prednisone.[27]

Systemic treatments

Corticosteroids

Although systemic corticosteroids are traditionally the main choice of treatment for BP, oral tetracycline antibiotics (ie, doxycycline) has demonstrated comparable efficacy with less adverse events. Tetracycline antibiotics are discussed below. Systemic corticosteroids are typically dosed at 0.5 to 0.75 mg/kg per day equivalents of prednisone. Tapering should be initiated 15 days after adequate disease control is achieved, ideally within 4 to 6 months of starting therapy.[25] In one trial, 50 patients were treated with either 0.75 or 1.25 mg/kg per day of prednisolone. At the 21-day mark, disease remission was achieved in 58% of patients in the lower dose group and 64% in the higher dose group, demonstrating noninferiority of the lower dose to the high dose.[28] To reduce the risk of adverse reactions, patients should be treated with the lowest dose of systemic corticosteroid needed to suppress the disease. In the older adult population, patients should also start calcium and vitamin D supplementation and bisphosphonate therapy. In addition, all patients should be screened for tuberculosis, with monitoring of their blood pressure and serum glucose levels.

Tetracycline antibiotics

Oral tetracycline antibiotics (eg, tetracycline, doxycycline, minocycline) should be strongly considered in patients with BP, especially in patients with contraindications to or intolerant of corticosteroid therapy. Doses are typically 1,500 to 2,000 mg/d for tetracycline, 200 mg/d for doxycycline, and 50 to 100 mg/d for minocycline.[25]

Among the tetracyclines, doxycycline is an especially strong candidate as an alternative to corticosteroids due to its potent

TABLE 2. DIFFERENTIAL DIAGNOSES OF BULLOUS PEMPHIGOID WITH DISTINGUISHING FEATURES

Differential Diagnosis[a]	Distinguishing Features
Bullous lupus erythematosus	- Occurs in patients with systemic lupus erythematosus (ANA, ENA, C3/4, anti-double-stranded DNA) - Blisters show preference for sun-exposed areas (can also be elsewhere) - Not always pruritic - Autoantibodies to type VII collagen
Dermatitis herpetiformis	- Triggered by gluten ingestion - Lesions are primarily symmetrical vesicles, not bullous, with predilection for extensor surfaces (elbows, knees, upper and lower mid back, scalp) - May have enamel pitting on teeth - Granular or fibrillar pattern of IgA deposition in papillary dermis or along basement membrane of perilesional skin
Epidermolysis bullosa acquisita	- Lesions are localized to trauma-prone and extensor surfaces - Lesions may resolve with scarring and milia formation - Progressive acral involvement may result in pseudosyndactyly - Scalp involvement may result in scarring alopecia - Autoantibodies to type VII collagen
Pemphigus foliaceus	- Crusted scaly lesions involving seborrheic regions (face and upper mid chest) - Usually localized - No blisters, does not involve mucosa - Positive Nikolsky sign (top layers of skin slip away when rubbed) - Autoantibodies to desmoglein-1
Pemphigus herpetiformis	- Annular-shaped distribution of lesions - Urticarial plaques - Does not involve mucosa - Autoantibodies to desmoglein-1
Pemphigus vegetans	- Typically presents with stomatitis (erythema and swelling of oral mucosa) - Blisters are flaccid, with formation of crusting vegetative plaques after rupture - Often positive Nikolsky sign - Autoantibodies to desmoglein-3 and often desmoglein-1
Pemphigus vulgaris	- Initial presentation usually involves oral mucosa and may be restricted to the oral mucosa - Blisters are flaccid - Positive Nikolsky sign - Autoantibodies to desmoglein-3 and/or desmoglein-1
Prurigo nodularis	- Predominant lesions are nodular, with predilection for extensor surfaces - No blisters, may have surface erosions - Often itchy - May experience burning and stinging

Abbreviations: ANA, antinuclear antibody; BP, bullous pemphigoid; DIF, direct immunofluorescence; ELISA, enzyme-linked immunosorbent assay; ENA, Extractable nuclear antigens; IgA, immunoglobulin A; IIF, indirect immunofluorescence.

[a]Laboratory investigations including histopathology, DIF, IIF, and ELISA can be used to differentiate differential diagnoses from BP.

anti-inflammatory effects. In one trial, 132 patients were treated with either doxycycline 200 mg/d or prednisolone 0.5 mg/kg per day. At the 6-week mark, 74% of patients treated with doxycycline had three or fewer blisters compared with 91% for prednisolone, demonstrating noninferiority of doxycycline to prednisolone. Furthermore, treatment-related severe, life-threatening, and fatal events occurred in 18% of doxycycline treated patients compared with 36% of patients treated with prednisolone.[29]

Tetracyclines can also be used in combination with nicotinamide (up to 2,000 mg/d). In a trial of 20 patients, treatment with tetracycline 2,000 mg/d combined with nicotinamide 1,500 mg/d was found to be equally as efficacious as treatment with prednisone 40 to 80 mg/d.[30]

Steroid-sparing immunosuppressive therapies

Several steroid-sparing immunosuppressive therapies are also available for patients who are intolerant or have contraindications to corticosteroids. They are also viable options in patients with recalcitrant BP that is inadequately controlled by corticosteroids as adjunctive therapies.

Azathioprine

For treating BP, azathioprine is typically dosed between 1 and 3 mg/kg per day.[25] Azathioprine is metabolized by thiopurine methyltransferase; thus, assessing the thiopurine methyltransferase level may aid in selection of dosage. In one trial, 25 patients were treated with prednisone 30 to 80 mg/d combined with azathioprine 2.5 mg/kg per day or prednisone 30 to 80 mg/d alone. At the 3-year follow-up, the addition of azathioprine was found to reduce the cumulative dose of prednisone by 45% without increases in serious adverse reactions or mortality.[31] Azathioprine has a slow onset of action and should be started in combination with corticosteroids during the acute phase of disease.

Methotrexate

Methotrexate is typically dosed between 5 and 12.5 mg/wk in treating BP.[25] In one trial, 300 patients were treated with topical

TABLE 3. TREATMENT OPTIONS FOR BULLOUS PEMPHIGOID

Topical Treatments	Systemic Treatments
Clobetasol propionate[a]	Corticosteroids[a]
Tacrolimus	Methylprednisolone
	Prednisolone
	Prednisone
	Tetracycline antibiotics ± nicotinamide[a]
	Doxycycline
	Minocycline
	Tetracycline
	Immunosuppressants
	Azathioprine
	Methotrexate
	Mycophenolate mofetil
	Biologics
	Dupilumab
	Omalizumab
	Rituximab

[a]First-line treatments.

clobetasol propionate in combination with methotrexate 10 to 12.5 mg/wk or topical clobetasol propionate alone. At the 4-week mark, the remission rate in the combination treatment group was 75% compared with 57% for the group treated with only topical clobetasol propionate ($P = .002$).

Mycophenolates

Mycophenolic acid is an inhibitor of lymphocytic proliferation and is available as mycophenolate mofetil and enteric-coated mycophenolate sodium. Both prodrug forms are rapidly metabolized to the active mycophenolic acid.[32] In treating BP, mycophenolate mofetil is typically dosed at 2,000 mg/d, whereas enteric-coated mycophenolate sodium is dosed at 1,440 mg/d.[25] In one trial, 73 patients were treated with methylprednisolone 0.5 mg/kg per day in combination with either mycophenolate mofetil 2,000 mg/d or azathioprine 2 mg/kg per day. Complete remission was achieved for all patients; however, the mean remission time in the azathioprine group was 23.8 days compared with 42.0 days for the mycophenolate mofetil group. Although azathioprine achieved more rapid remission, it had higher rates of adverse reactions, with 24% of azathioprine-treated patients experiencing a grade 3 or 4 adverse reaction compared with 17% of patients treated with mycophenolate mofetil.[33]

Dapsone

Dapsone in doses of up to 1.5 mg/kg per day may be used in patients with contraindications to corticosteroids or other immunosuppressants or to reduce the cumulative dose of corticosteroids and may be particularly effective if histologic analysis reveals predominance of neutrophils.[25] In one trial, 54 patients were treated with methylprednisolone 0.5 mg/kg per day in combination with either dapsone 1.5 mg/kg per day or azathioprine 1.5 to 2.5 mg/kg per day. The median cumulative dose of corticosteroid for the patients treated with dapsone was 1.92 g compared with 2.65 g for azathioprine ($P > .05$), demonstrating noninferiority of dapsone to reduce cumulative dose of corticosteroid compared with azathioprine.[34]

Biologics

Biologics may be considered in patients with BP recalcitrant to other therapies or who have contraindications to other therapies. Biologics may be used as monotherapy or in conjunction with other therapies.

Dupilumab

Dupilumab is an interleukin 13/interleukin 4 inhibitor used in treating atopic dermatitis. In a retrospective chart review, 24 patients were treated with dupilumab in addition to methylprednisolone 0.6 mg/kg per day and azathioprine 2 mg/kg per day or methylprednisolone and azathioprine alone. The median time to cease new blister formation was 8 days in the dupilumab group compared with 12 days for the methylprednisolone and azathioprine-alone group. The median cumulative dose of methylprednisolone in the dupilumab group was 1,898 mg compared with 2,344 mg for the methylprednisolone and azathioprine alone group. These results suggest that the addition of dupilumab can provide a potential steroid-sparing effect and cease new blister formation more rapidly.[35]

Omalizumab

Omalizumab is a monoclonal antibody targeting IgE used in treating asthma and spontaneous idiopathic urticaria. In a systematic review, 56 patients were treated with omalizumab either as monotherapy or in combination with other therapies. Of these patients, 55.4% achieved complete remission, and 32.1% achieved partial remission.[36] Omalizumab may be particularly effective in treating patients with BP who have urticarial lesions and high serum IgE levels.[25]

Rituximab

Rituximab is a monoclonal antibody targeting CD20 on B cells used in treating certain hematologic malignancies and autoimmune diseases. In a retrospective chart review, 20 patients were treated with rituximab in conjunction with other therapies, most commonly prednisone. Of these patients, 75% achieved remission after an average of 169 days.[37]

IV immunoglobulins

IV immunoglobulins (IVIgs) are concentrated collections of antibodies pooled from large numbers of donors that have been used to treat humoral immunodeficiency and autoimmune conditions. In a trial involving 53 patients with BP whose disease did not improve on oral prednisolone >0.4 mg/kg per day, those treated with IVIg 400 mg/kg per day adjuvant therapy for 5 consecutive days achieved improvements in disease activity score compared with placebo, but did not reach statistical significance.[38] However, IVIg may be of therapeutic benefit in treatment-resistant cases of BP.

WOUND CARE

Medical treatment must be combined with appropriate wound care to prevent loss of skin integrity and reduce risk of infection. Cleanse blisters with 0.9% sodium chloride, and use a needle to make punctures and small incisions on each side of the blister. Apply soft pressure with a gauze pad to drain the blister. The roof of the blister should be left in place to prevent the underlying skin from being exposed to the surrounding environment, which can be painful and increases risk of infection. Once drained, dry blisters to prevent new outflow of fluid. Silver nitrate 1% solution on a gauze pad can be used to assist in the drying process; however, this may be painful for some patients.

Topical corticosteroids can then be applied with an ointment base under a petroleum jelly tulle dressing if required. A gauze pad and wrap bandages can be applied on top to protect the skin from trauma, which is especially important because of the increased fragility of skin from corticosteroid use. If there are signs of infection (eg, pain, malodor, erythema, fever), blisters should be cleaned with antimicrobials and cultures taken to determine the source of the

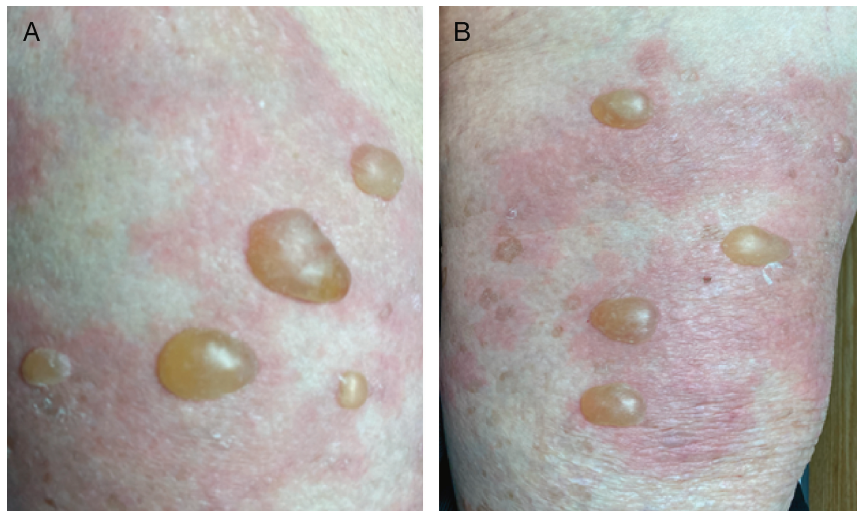

FIGURE 2. CASE EXAMPLE
Tense clear blisters on an erythematous base with islands of sparing on the (A) anterior right thigh and (B) anterior left thigh. The patient provided permission for the images to be published.

infection (eg, *Staphylococcus aureus*, herpes) and treated with appropriate medication.

EXAMPLE CASE

A 71-year-old woman presented with tense, clear blisters on an erythematous base with islands of sparing involving the bilateral anterior thighs. The initial onset consisted of papular lesions that evolved over 3 weeks to the current presentation shown in Figure 2. With the suspicion of BP, a biopsy was taken for direct IIF, which revealed linear deposition of IgG at the dermoepidermal junction. Serology investigations revealed elevated IgE, eosinophilia, and an anti-BP autoantibody titer of 1:80. With the history and investigations being supportive of a diagnosis of BP, the patient was started on prednisone 0.5 mg/kg per day after a negative tuberculin skin test. An oral antihistamine was also provided to manage pruritus (cetirizine 20 to 40 mg at night). The patient was counseled to start calcium, vitamin D supplementation, and bisphosphonate therapy. Blood pressure and serum glucose levels are being monitored, and therapeutic response will be assessed in 1 month.

CONCLUSIONS

Bullous pemphigoid is a subepidermal blistering disease that is usually observed in the older adult population and is rarely seen in children. The physical discomfort (intense pruritus) and physical appearance of lesions result in psychosocial burden on patients, including depression, negative body image, and social isolation. Therapies with efficacy in treating BP have anti-inflammatory or immunosuppressive properties, with topical or systemic corticosteroids being the primary choice of treatment. However, choice of therapy should be made with consideration of patient age, comorbidities, and concurrent medication use.

PRACTICE PEARLS

- Bullous pemphigoid is the most common subepidermal blistering disease, mainly observed in patients older than 70 years.
- Classic BP is characterized by tense blisters on normal skin or erythematous base, often on flexor surfaces.
- There are several rare clinical variants of BP that vary in lesion localization, lesion type, and age at onset.
- The criterion standard for diagnosing BP is with direct IIF for detection of linear deposition of IgG or C3 at the dermoepidermal junction and/or indirect IIF for IgG at the basement membrane zone.
- Therapies with anti-inflammatory or immunosuppressive properties are efficacious in treating BP; topical or systemic corticosteroids are the primary choice of treatment. A large, controlled study demonstrated doxycycline 100 mg BID was not inferior to systemic corticosteroids and was associated with fewer severe adverse effects, including fewer deaths.[29]

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