



Case report

Bullous Pemphigoid After Total Knee Arthroplasty

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ABSTRACT

Total knee arthroplasty is one of the safest and most routinely performed orthopedic procedures. As the volume of cases is expected to rise each year, so too will the incidence of uncommon complications. We describe a rare case of bullous pemphigoid, an autoimmune skin blistering disorder, that occurred after total knee arthroplasty in an otherwise healthy patient and led to hospital readmission. Early diagnosis and treatment of this condition may limit its spread and help to avoid comorbid sequelae.

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Introduction

Total knee arthroplasty (TKA) is one of the most common orthopedic procedures. Roughly 400,000 cases are performed annually in the United States [1], a number that is expected to increase by 85% within the next decade [2]. It is therefore important to increase awareness and recognition of rare postoperative complications.

Bullous pemphigoid (BP) is an autoimmune subepidermal disease characterized by intensely pruritic, fluid-filled blisters [3]. Common precipitating factors include viral infection and certain medications in genetically susceptible individuals [4]. However, there are a limited number of reports of postsurgical BP in the literature [5–13], with only 4 reports of BP after TKA [14–17]. Herein, we present a rare case of generalized BP after routine TKA in a 73-year-old male, leading to rehospitalization.

The patient was informed that information regarding his case would be submitted for publication and provided his consent.

Case history

A 73-year-old male underwent left TKA for the treatment of tricompartmental degenerative joint disease (Fig. 1). Past medical history included hypertension, hyperlipidemia, gastroesophageal reflux disease, obesity, obstructive sleep apnea, and prediabetes mellitus. Daily medications were amlodipine, rosuvastatin, and omeprazole. Intraoperative blood loss was 100 mL, and tourniquet time was 70 minutes at 250 mmHg. Short-acting spinal anesthesia was used. No peripheral nerve blocks or intra-articular injections (corticosteroids, viscosupplements, blood-derived products) were provided for adjunctive pain management. The medial parapatellar arthrotomy was closed with 1-0 coated polyglactin 910 (Vicryl; Ethicon Inc, Somerville, NJ). The skin was approximated with 0-0 Vicryl and 2-0 Vicryl subcutaneously and closed with 3-0 poliglecaprone 25 (Monocryl; Ethicon Inc, Somerville, NJ) and 2-Octyl cyanoacrylate skin adhesive (Dermabond Prineo; Ethicon Inc, Johnson and Johnson, Somerville, NJ). A foam dressing with an adhesive silicone layer (Mepilex Border; Mölnlycke Healthcare, Gothenburg, Sweden) was applied. The patient was discharged on day 1 without complications. He was prescribed 5-mg oxycodone every 4–6 hours as needed for pain and 325-mg aspirin twice daily for deep vein thrombosis prophylaxis.

On postoperative day 10, the dressing was removed, and the incision site was clean, dry, and intact. Range of motion (ROM) was

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Figure 1. Antero-posterior (a) and lateral (b) preoperative radiographs and antero-posterior (c) and lateral (d) postoperative radiographs.

5° to 95°, and the patient was meeting home physical therapy goals. On postoperative day 14, the patient developed erythema and pruritus of the medial aspect of the operative knee and distal thigh. He denied fever, chills, or knee pain at that time. The patient's primary care physician started him on 500-mg Keflex 4 times per day for suspected cellulitis. On postoperative day 17, he presented to the emergency department with tense, intensely pruritic bullae on the medial aspect of the operative knee and distal thigh (Fig. 2a).

He was afebrile at this time, without evidence of leukocytosis. Radiographic evaluation revealed neutral alignment of the knee and well-seated components without sign of surrounding lucency. He was admitted by the medical service and treated with

intravenous ceftaroline, diphenhydramine, and loratadine. On postoperative day 20, he developed a new urticarial and vesicular rash on his abdomen and bilateral flanks and axillae (Fig. 3).

Antibiotic administration was discontinued because of concern for a drug eruption. The patient was started on 60 mg of prednisone daily and 0.05% clobetasol topical cream twice daily. A bedside skin biopsy was performed, revealing a subepidermal blister with eosinophils and adjacent ulceration and re-epithelialization. Direct immunofluorescence confirmed the diagnosis of BP. No change in postoperative rehabilitation protocol was initiated once the diagnosis of BP was made and treatment was initiated. On postoperative day 22, upon stabilization of the rash, significant decrease in

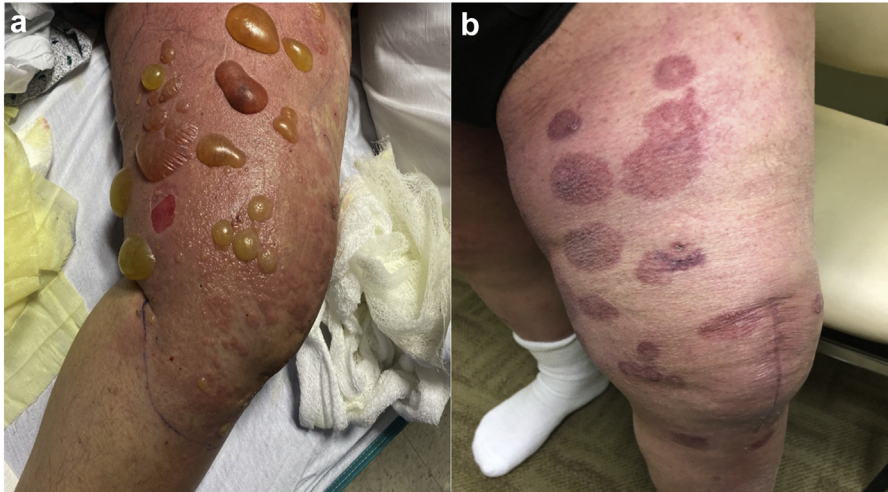


Figure 2. Left medial leg 17 d after TKA, showing 20 tense, serous, and serosanguinous bullae and one erosion (a). Left medial leg 3 mo after TKA, showing postinflammatory hyperpigmentation (b).

pruritus, and no signs of secondary infection, the patient was discharged and instructed to follow up with a dermatologist. At his 3-month postoperative visit, all bullae and pruritus had resolved, and the midline incision had appropriately healed (Fig. 2b). Knee pain was 3 out of 10, and ROM was 2.5° to 120° with 5 out of 5 strength with resisted flexion and extension. Prednisone and clobetasol were discontinued at this time. At his 6-month postoperative visit, the patient exhibited full strength and ROM of his operative knee without recurrence of skin lesions. No complications related to prolonged corticosteroid therapy were experienced. He was satisfied with his outcome and instructed to follow up as needed.

Discussion

BP is the most frequently encountered autoimmune bullous disease. Its pathogenesis involves a dysregulated cellular and humoral immune response against hemidesmosomal proteins within the basement membrane [3]. Most commonly, BP is characterized by severe pruritus, followed by the appearance of tense bullae and vesicles over urticarial plaques on the trunk and extremities. Erosions and crusting may occur, but mucosal involvement is

uncommon. Diagnosis relies on histopathological findings of eosinophilic spongiosis or a subepidermal detachment with eosinophils; linear deposition of IgG or C3 at the basement membrane using direct or indirect immunofluorescence; and antibodies against BP180 or BP230 using ELISA [3].

To our knowledge, only 4 other cases of BP after TKA have been reported [14–17] (Table 1). All reports documented a consistent description of the rash: intensely pruritic, tense, fluid-filled blisters on an erythematous base. However, the onset of disease, presenting site, and localization of spread were varied.

Among all cases, the onset of BP after TKA ranged from 2 days to 9 months postoperatively. In addition to the case of our patient, who was diagnosed with BP 20 days postoperatively, only one other published report involves a diagnosis of BP in the acute postoperative period. Kim et al. described a case of generalized BP that started 3 days after surgery and spread to the operative knee 1 week later [14]. Skin biopsy confirmed a diagnosis of BP, prednisolone 10-mg was administered twice daily, and lesions completely resolved in 4 months. The same patient underwent TKA of the contralateral knee 1 year later, resulting in recurrence of the same symptoms 2 days postoperatively. A representative lesion was

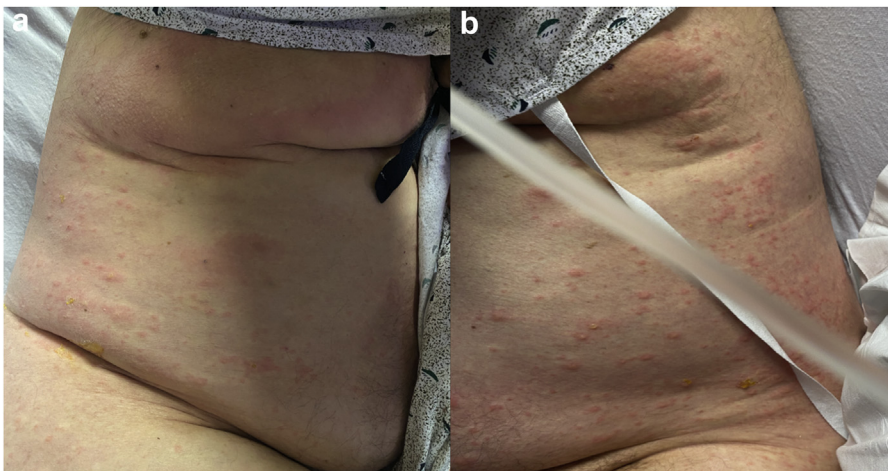


Figure 3. Right (a) and left (b) ventrolateral trunk showing patchy erythema, diffuse wheals, and 10–15 overlying vesicles on his abdomen, flanks, and axillae. Excoriation and serous crusting can be observed over some lesions.

Table 1
Previously reported cases of BP after TKA.

Case	Patient age, sex	Surgery	Onset and site of primary lesions	Onset and site of diffuse progression	Treatment and duration leading to remission	Readmission
Present study	73, M	L TKA	17 d—operative knee and distal thigh	20 d—abdomen, bilateral flanks and axillae	Clobetasol cream 0.05% BID +60 mg prednisone daily (3 mo)	Yes
Kim et al. [14], 2021	75, M	L TKA R TKA	3 d—buttocks and thighs 2 d—buttocks and thighs	10 d—operative knee and forearm No spread after treatment	Prednisolone 10 mg BID in both cases (4 mo vs 2.5 mo)	No
Kosi et al. [15], 2016	74, M	R TKA	9 mo—operative knee	No spread	Clobetasol cream 0.05% BID (8 wk)	No
Truss et al. [16], 2019	85, F	R TKA	2 d—operative knee	5 mo—contralateral foot, hips, and bilateral hands	Topical betamethasone + fucibet + trimovate (unknown)	No
Kavak et al. [17], 2006	72, F	L TKA	No localized primary lesions	5 mo—operative knee, bilateral feet, and back	Deflazacort 48 mg daily + nicotinic acid + topical steroid (unknown)	No

immediately biopsied, once again confirming a diagnosis of BP. By initiating the same treatment earlier (2 days postoperative vs 10 days postoperative), the eruption resolved 1.5 months sooner and did not spread to the surgical site. The remaining cases in the literature describe delayed presentations of BP at 5 and 9 months after surgery [15–17].

After TKA, the primary site of the bullae was either confined to the periphery of the surgical incision or generalized to include remote areas. Local lesions had a predilection for spread in all but one case [15]; common areas of generalization included the extremities, axillae, hips, buttocks, thighs, and abdomen. The onset of diffuse spread after the appearance of the localized rash ranged from 3 to 7 days.

Treatment included topical steroids alone, systemic steroids alone, or a combination of topical steroids and systemic steroids. The patient with local disease was treated with topical steroid alone, resulting in resolution of disease by 2 months [15]. Those with generalized BP were treated with either systemic steroids or combination therapy, resulting in resolution between 2.5 and 4 months [14]. Early treatment may reduce time to eradication and prevent additional spread of lesions [14].

When working up a patient with bullae or vesicles appearing after a TKA, it is important to consider a complete differential diagnosis, including but not limited to BP, postoperative skin blistering, allergic contact dermatitis (ACD), and bullous cellulitis. In the case of our patient, the initial working diagnosis was routine postoperative skin blistering—the incidence of which ranges from 2.1% to 41% [18]. Similarly, Truss et al. described an acute presentation of peri-incisional vesicular lesions that developed 2 days after surgery [16]. The patient tested negative for BP at 6 weeks, and it was concluded that the initial localized vesicular lesions were likely secondary to postoperative soft-tissue swelling opposed to autoimmune pathology. Interestingly, the lesions had generalized at 5 months, and a diagnosis of BP was finally confirmed. Many factors unique to arthroplasty account for postoperative skin blistering without autoimmune etiology. First, intraoperative manipulation of the knee results in significant postoperative soft tissue edema. Second, incisions overlying joints result in skin movement during wound healing. Finally, long-term use of wound dressings causes tension at the skin-dressing interface, weakening the dermo-epidermal connection [18].

Surgical site infection may present as a bullous cellulitis and must also be considered in postoperative patients who acquire rapidly spreading vesicular lesions around their incisions [19]. Most patients who developed BP after TKA were treated with antibiotics for presumed soft-tissue infection—a likely reaction to erythema and persistent blister formation about the operative knee. Moving forward, however, BP should be more heavily considered in afebrile

patients with tense, intensely pruritic blister formation without evidence of purulent drainage or leukocytosis.

Another rare cause of acute bullous reactions after TKA is ACD. A 0.05% incidence of ACD is associated with 2-octyl cyanoacrylate (Prineo), a common skin adhesive used for wound healing after TKA, and a component of the skin closure system that was used on our patient [20]. Reactions occur 5 to 14 days after application and may present with diffuse, pruritic, bullous lesions in severe cases [20]. Removal of adhesive, daily dressing changes, and topical steroids should result in complete remission. If disease continues despite these precautions, BP should be considered. None of the other reports involved the use of Prineo dressings [14–17].

Despite positive outcomes in each of the patients described here and in the literature, the prognosis of BP is not always favorable. Overall mortality is 2 to 7 times greater than that among age and sex-matched controls, and a recent meta-analysis estimates a 23.5% mortality rate in the first year after diagnosis [21]. This statistic is likely driven by confounding variables, such as patient age, medical comorbidity [22], oral steroid treatment [23], and secondary infection leading to sepsis [24], opposed to the disease itself. With the exception of our patient, none of the patients reported were readmitted for this complication. Importantly, no mention of a periprosthetic joint infection or a clinical deficit in postoperative knee function with regard to ROM, strength, pain level, or need for ambulatory assist devices was presented in the other studies [14–17].

Summary

Orthopedic surgeons should be familiar with BP symptomatology and its presentation in the acute and chronic periods after TKA. Prompt biopsy, dermatology consultation, and treatment may shorten the disease course and thereby reduce readmission rates, improve patient satisfaction, and reduce morbidity of this rare postoperative complication.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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