



## Medical Science

# Bullous Pemphigoid Triggered by Surgery for Hip Replacement

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### Abstract:

Bullous Pemphigoid (BP) is a rare immune-mediated disease that occurs with recurrent exudative lesions. Despite the genetic determination, the clinical manifestation of the disease is mainly in old age. A number of triggers have been described in the literature, including exposome factors, medications, vaccines, trauma, and a number of others. On the other hand, in most of the cases the trigger factor remains unspecified. We present a case of a 76-year-old patient diagnosed with BP. The disease began 2 weeks after the surgery for hip replacement with the appearance of bullae on the skin at the site of surgical intervention.

**Keywords:** bullous pemphigoid, rare disease, trigger factor, artificial hip

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### Introduction:

Bullous Pemphigoid (BP) is a rare autoimmune disease that occurs with recurrent exudative lesions. The basis of the pathogenesis is the formation of autoantibodies directed against the hemidesmosomes, the rupture of which results in the formation of subepidermal bullae. The incidence of the disease is between 2.4 to 23 cases per million with a clear tendency to increase [1]. Current studies point to a relationship between the course and the severity of BP and neurologic disorders, vitamin D deficiency and thrombosis [2]. Among the trigger factors the most often mentioned are drugs, physical factors, underlying cancers, infections, transplantations, and others [3]. There are also quite a few cases of BP with an unclear trigger mechanism. Diagnosis is based on clinical, histological and immunological findings.

However clear criteria for distinguishing the different subtypes of the disease are still missing [4]. Among the factors responsible for the appearance of BP are exposome factors as well. The share of physical factors is relatively small and mostly there are various traumas, including surgical interventions [3].

### Presentation:

We present a 76-year-old Caucasian male patient who was hospitalized for blisters spread over the body and the right hip. The rashes appeared a few days ago, initially few and gradually increasing in number. On admission, the patient complained of severe itching and pain causing sleep disturbance. His general condition is not affected. Three months earlier, he underwent an operation for the

replacement of the right hip joint. From his medical history: without comorbid conditions.

The dermatological status showed disseminated rash on the extremities and single lesions in the trunk area (Fig.1), as well as clustered lesions overlying the skin of the right hip joint (Fig.2). There were tense bullae with clear to hemorrhagic contents on the dorsum of the left foot as well.



**Fig.1 Skin lesions on the trunk.**

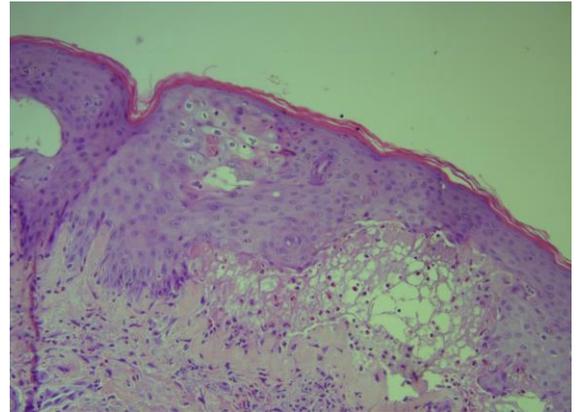


**Fig. 2 Clustered skin lesions on the right hip.**

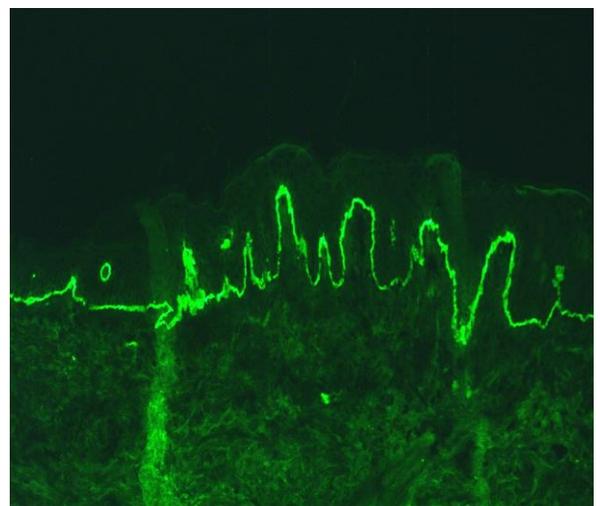
The Ro graph of the lung was normal. No deviation was observed in the blood count, except for CRP, which was slightly elevated.

An excisional biopsy from the lesion was performed. Histopathology revealed a subepidermal bulla with eosinophilic leukocytes in the cleft, in the superficial dermis presence of lymphoplasmatic infiltrates mixed with numerous eosinophilic leukocytes and single histiocytes in places located perivasally (Fig. 3). Direct immunofluorescence showed linear deposits of C3

on the dermo-epidermal border (Fig. 4). A diagnosis of bullous pemphigoid was made.



**Fig. 3 Sub-epidermal blister with eosinophilic leukocytes in the bullae.**



**Fig. 4 Linear deposits of C3 on dermo-epidermal border.**

The improvement of symptoms started after corticosteroid treatment, which started with an initial dose of 60 mg/day, followed by reduction by 10 mg daily and azathioprine 2x50mg per day. The patient responded well to this course of treatment and is currently in remission on a maintenance dose of azathioprine 50mg per day.

#### **Discussion:**

BP is a rare autoimmune bullous disease. The clinic is dominated by the presence of tense vesicles and bullae, accompanied by itching and pain. The pathogenic substrate of the dermatosis is the formation of autoantibodies directed against proteins (anti-BP180/230), involved in the construction of the lamina lucida of the zone of basement membrane. The disease is mainly

observed in older patients, which correlates with the age of the patient we present. It often occurs spontaneously, but numerous precipitating factors have also been described in the literature. The most numerous are the data on drug-induced and drug-triggered BP. Among the plethora of medications cited in the literature are antibiotics, diuretics, TNF- $\alpha$  Inhibitors [5, 6], and others more than 89 drugs [7]. The mechanism of occurrence of drug-induced BP is still debatable. Vassileva describes a case of contact BP after local use of medication as irritation and allergic contact hypersensitivity are indicated as a likely provoking mechanism for the BP induced by topical medications [8]. In the literature we found case reports of BP after vaccines [9]. Among other triggering factors should be mentioned different infections [10]. A number of physical factors have been cited as possible triggers for the occurrence of BP [3]. Chen D. and co-authors presented a case of BP induced by chemical burn [11]. Mai and coauthors reported that surgical procedures act as a trigger factor in 37% of all physical factors [12]. In their study, Dănescu and co-authors analyzed nine cases of BP and pointed out that surgical procedure could act as a trigger [13].

Hip replacement is a routine surgical intervention for osteoarthritis. Like any surgical intervention, it can be followed by general or procedure-specific complications [14]. Samuel and coauthors describe a rare complication of joint replacement due to metal hypersensitivity [15]. There are a few case reports of BP after total knee arthroplasty [16].

The case presented by us concerns clinically, histologically and immunologically diagnosed BP in a patient without comorbidities. The occurrence of the disease in an immediate short time interval after hip replacement, as well as the presence of lesions at the site of the surgical procedure, give us reason to assume that it is a case of BP induced by surgery for hip replacement. We found just one reported case of BP triggered by surgery for hip replacement [17]. When surgical procedures act as a trigger factor for BP the blisters could be localized at the site of intervention or spread over distant areas of the skin [3]. In the case presented

by us, exudative lesions were observed both directly in the area of surgical intervention and in more distant places of the body surface. It is still debatable whether the triggering factor is the surgical procedure itself or a hypersensitivity reaction to the material from which the artificial joint is made.

### Conclusion:

BP is a relatively rare autoimmune bullous dermatosis. It predominantly affects elderly individuals. In many cases, the initial appearance can be provoked by internal or external factors of the environment. In the available literature, we found just few reported cases of BP triggered by joint replacement. We believe that the case presented by us of the patient with BP provoked by hip replacement surgery is interesting and would be useful for both dermatologist and surgeons.

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