



A Case of Bullous Pemphigoid Related to Allograft Renal Rejection in a Young Female

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Abstract

A 24-year-old young female developed Bullous Pemphigoid (BP). This patient received a transplanted kidney from her mother because of chronic renal failure. She developed chronic humoral immune transplant rejection (chronic renal rejection) four months before developing BP, and her BP started at the same time as acute cell-mediated immune graft rejection (acute renal rejection). After one month of BP treatment, her BP showed improvement, but the titer of anti-BP 180 non-collagenous 16a (NC16a) antibody remained in a high range. The recrudescence of her BP would be cause for concern is apprehensive because of the high titer of anti-BP 180 NC16a antibody. Type XVII collagen (BP180) is a common antigen between the skin and kidney. Her BP and the high titer of anti-BP 180 NC16a antibody might be related to the transplant tissue. We were concerned about the recurrence of the BP, and we removed the transplanted kidney. After three weeks of nephrectomy, her skin condition was improved, and the anti-BP 180 NC16a antibody titer was quickly reduced. We present the case of BP in a young female, and six other cases of BP in younger people (less than 30 years old) related to the rejection of a transplanted kidney have been reported.

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Introduction

Bullous Pemphigoid (BP) usually occurs in elderly people, and cases of this disease in individuals younger than 30 years old are rare. Diseases that can be comorbid with BP include Diabetes Mellitus (DM), dementia, Parkinson's disease, autoimmune diseases [1,2], and psoriasis vulgaris [3,4]. Cases of BP related to renal transplantation are rare, with a total of seventeen such cases having been reported [5-20] (Table 1). Only six BP cases related to renal transplant rejection in individuals less than thirty years old have been reported in addition to our case (Table 1) [5,6,8,11,12,15]. These BP cases might be related to immune cross-reactivity between epidermal and glomerular basement membrane antigens [21]. One effective treatment for BP related to renal allograft rejection is nephrectomy.

Case Presentation

A 24-year-old female developed bullas, erosion, and erythema on her whole body, and her skin condition did not improve. She had not been eating well due to oral mucous and tongue erosion, and her skin condition worsened. Our diagnosis was BP based on the clinical findings (Figure 1a), the results of skin biopsy (subepidermal bulla and mainly lymphocytes and eosinophils infiltrate, superficial and deep perivascular dermatitis) (Figure 1b), and the high titer of anti-BP180 non-collagenous 16a (NC16a) antibody (2980 U/ml) (Figure 1c). The Bullous Pemphigoid Disease Area Index (BPDAI) scores were bulla and erosion 53/120, erythema 30/120, and mucous membrane 11/120.

Her medical history is as follows. Chronic renal failure of unknown origin started at thirteen years of age, and she received renal transplantation from her mother nine years ago. The origin of her chronic renal failure was not detected. She developed chronic humoral immune transplant

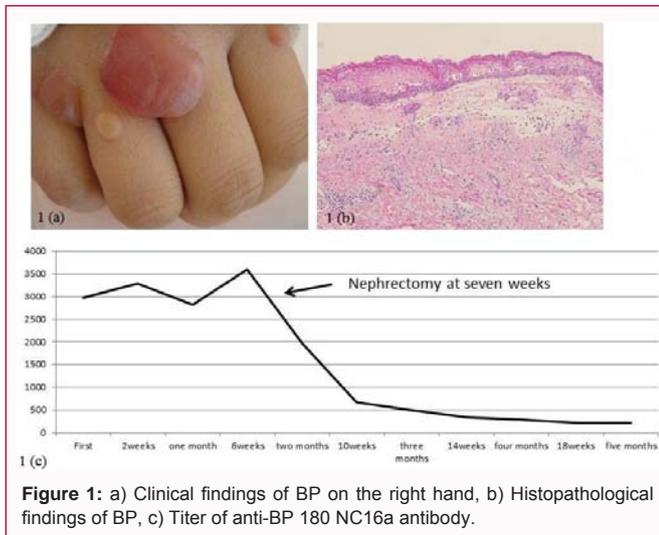


Figure 1: a) Clinical findings of BP on the right hand, b) Histopathological findings of BP, c) Titer of anti-BP 180 NC16a antibody.

rejection (chronic renal rejection) and restarted dialysis beginning at twenty three years of age, and then (after four months) she developed acute cell-mediated immune graft rejection (acute renal rejection) and BP at twenty four years old.

We began treating her BP using steroid ointment, steroid tablets (prednisolone 15 mg/day; 7.5 mg/day for immunosuppression and 7.5 mg/day for BP treatment) and antihistamine tablets. After one month of treatment, her skin condition and BPDAl score improved, although her anti-BP180 NC16a antibody titer remained high (2820 U/ml) (Table 1). Because the high titer of BP-180 NC16a antibody might have been caused by the transplanted kidney, we removed the transplanted kidney at seven weeks of BP treatment. After the allograft was removed, the titer of BP-180 NC16a antibody quickly decreased. Thirteen weeks after the transplanted kidney was removed, her skin condition was good (BPDAl score: Bulla 0/120, erythema 0/120 and mucous membrane 0/120) and then the dose of steroid gradually were decreased with the improvement of her skin condition and the titer of BP-180 NC16a antibody (Table 1).

Discussion

Generally, BP is a chronic autoimmune blistering skin disease in elderly people. Patients with BP usually contract comorbid diseases such as DM, dementia, Parkinson's disease, or autoimmune diseases. Our patient did not exhibit any of these comorbid diseases. Based on the course of her BP, the development of BP in this case might have been related to chronic and acute renal rejection and we speculated that our patient's BP was caused by an immune cross-reaction between her skin and allograft kidney. The target of the autoimmune reaction in BP is located in the skin, basement membrane, and hemidesmosome [22]. There are three protein molecules, namely plectin, BP 230, and BP180 (Type XVII collagen: BPAg2) in the extracellular components of the basement membrane. Type XVII collagen (BPAg2) is a component of hemidesmosome, an adhesion molecule in the skin basement membrane. The main target of BP is type XVII collagen (BP180) [22], and many BP patients possess autoantibodies against the extracellular NC16a domain of collagen XVII [23-25]. Recently, type XVII collagen was detected in the glomerular basement membrane [26] in a report that connected skin and kidney immune reactions. Matsumura [27] reported that anti-basement membrane autoantibodies react with the NC16a domain of BPAg2. The titer of anti-BP 180 (anti-BPAg2) antibodies is used to determine the

Table 1: Cases of BP related to renal allograft rejection.

Age	Sex	Type of Graft Rejection Reaction	Reference No
10	F	Chronic	[5]
9	M	Chronic	[6]
15	F	Chronic	[8]
27	M	Chronic	[11]
13	M	Chronic	[12]
15	F	Chronic	[15]
25	F	Chronic_Acute	Our case
47	F	Chronic	[7]
52	M	Chronic	[9]
46	M	Acute	[10]
50	M	Chronic	[12]
39	M	Chronic	[14]
59	F	Chronic	[16]
34	F	Chronic	[17]
49	M	Chronic	[17]
32	M	Unknown	[18]
63	M	Acute	[19]
46	F	Chronic	[20]

activity of BP [28]. Patients with DM, dementia, Parkinson's disease, and autoimmune diseases may be at risk of developing BP if they possess a positive titer of anti-BP 180 antibodies. Suzanne et al. [12] described that the occurrence of anti-BPAg2 antibodies may be secondarily triggered by the initial cutaneous aggression through the phenomenon of epitope-spreading. Hashimoto et al. [29] found that the analysis of epitope-spreading in skin diseases may provide insight into pathogenic mechanisms in transplantation immunity. Type XVII collagen was detected in the glomerular basement membrane [26], and it is a common antigen between the skin and kidney. In these reports, type XVII collagen (BPAg2) is an essential antigen in the mechanisms of epitope-spreading in BP in patients with transplanted tissue. We speculate that antibodies against the BP-180 antigens in the skin and glomerular basement membrane could have been produced *via* epitope-spreading during chronic renal rejection, and an immune reaction between BP antigens and anti-BP180 antibodies might have been provoked during acute renal rejection in this case. A quick decrease of the titer of BP-180 NC16a antibody occurred after the nephrectomy, and this suggests that the slow change of the titer of BP-180 NC16a antibody after the skin improved could be related to the allograft kidney. Patients with BP sometimes develop comorbid diseases, possibly due to the presence of type XVII collagen in the bladder, buccal mucosa, conjunctiva, and neurons of the central nervous system, ocular cornea, placenta, retina, upper esophagus, and umbilical cord [30-33]. Careful observation of elderly people with diseases in these tissues is needed, with a focus on the potential for developing BP.

Conclusion

A 24-year-old young female developed bullous pemphigoid related to allograft renal rejection with the high titer of anti-BP180 NC16a antibody. After the nephrectomy, her skin condition was improved, and the anti-BP 180 NC16a antibody titer was quickly reduced.

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