A Case of Bullous Pemphigoid with Hypothyroidism Caused by Hypopituitarism

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Abstract: A case of bullous pemphigoid with hypothyroidism caused by hypopituitarism is reported. The patient had a history of brain infarction six years ago. Over three months, tense vesico-bullous eruptions developed on her whole body. Histopathology revealed subepidermal blisters with dense eosinophil infilitrations. A direct immunofluorescent study found deposition of IgG and C3c components in the basement membrane zone. A blood examination showed greatly elevated titer of BP 180 antibody. Based on clinical, histopathological and laboratory findings, the patient was diagnosed as bullous pemphigoid. In our examination of endocrine functions, reduced levels of ACTH, TSH, FT3, FT4 and aldosterone were found, suggesting hypothyroidism caused by hypopituitarism. After the patient was treated by corticosteroid pulse therapy (methylpredonisolone 500mg/d with tapering), the lesions improved. Neurological examination showed lacuna infarction in the brain. We reported a case with bullous pemphigoid with hypothyrodism caused by hypopituitarism.

Keywords: Bullous pemphigoid, hypothyroidism, hypopituitarism.

INTRODUCTION

Bullous pemphigoid (BP) is an autoimmune bullous disease. The etiology of BP is not clear. BP occurs predominantly in elderly persons. Autoantibody against basement membrane zone is responsible for the formation of subepidermal bulla in BP. High prevalence of neurological disorders in patients with BP has been reported [1]. To interest, unilateral bullous pemphigoid limited to hemiplegic sites has been reported [2]. The concomitant complication between BP and brain infarction has been reported [2]. Synopsy of brain infarction has been reported [3].

We describe a patient who had a previous history of brain infarction before and subsequently developed onset of BP with analysis in endocrine function.

CASE REPORT

In May, 2011 a 59 years old woman experienced a vesico-bullous eruption on the whole body. Clinical findings were tense bulla, vesicles with exudative erythema, purpura, crust and erosion on her entire body (Figure **1**). Hemiparesia was not observed.

Histopathological findings demonstrated that subepidermal blisters with dense eosinophilic and neutrophilic infiltrations were observed in the upper dermis with edema and dilated vessels (Figure **2**). A direct immunofluorescent (IF) study showed the linear band of IgG (Figure **3**) and C3c deposition in the basement membrane zone. IgM, IgA, C1q and fibrinogen were negative. We observed elevated white blood cell (WBC) count of 15100/μl with a left shift due to neutrophil (80%). And increased platelet (52.7×10^4 /μl) were observed. The titer of BP 180 antibody was more than>150, and antibodies against desmoglein-1 and desmoglein-3 were negative (ELISA: SRL). Liver enzymes were high: (LDH 270IU/l, Alp 548IU/d, g-GTP 78IU/l, and LAP 75IU/l). Choline esterase (ChE) was decreased. C-reactive protein (CRP) was elevated (5.84mg/dl). Renal functions are disturbed (Blood urea nitrogen 27.3mg/dl, Creatinine 0.87mg/dl). The level of serum IgG was decreased (597mg/dl). Anti-nuclear antibody (ANA) was negative. Bacterial culture from the

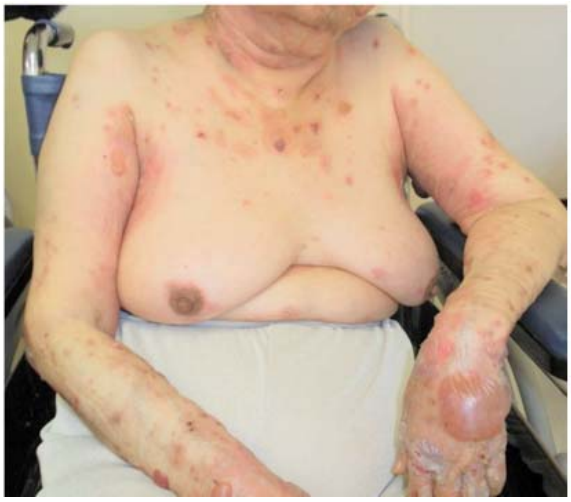

Figure 1: Tense bulla, vesicles, exudative erythema, purpura, crust and erosion on the whole body.

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lesions; *Methicillin resistant Staphylococcus aureus* (*MRSA*) was detected.

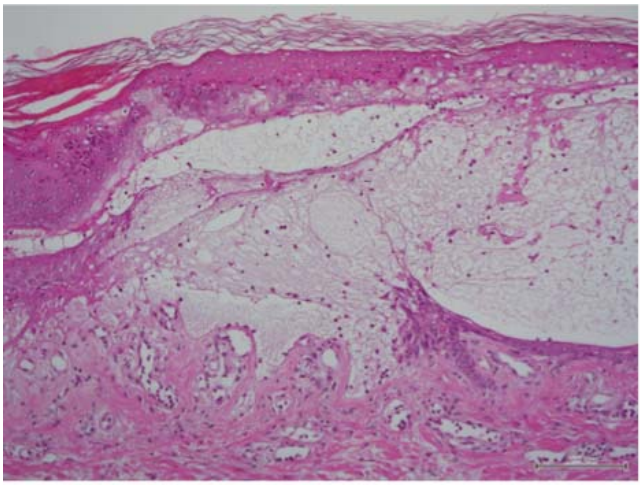

Figure 2: subepidermal blisters with dense eosinophilic and neutrophilic infiltrations were observed in the upper dermis with edema and dilated vessels.

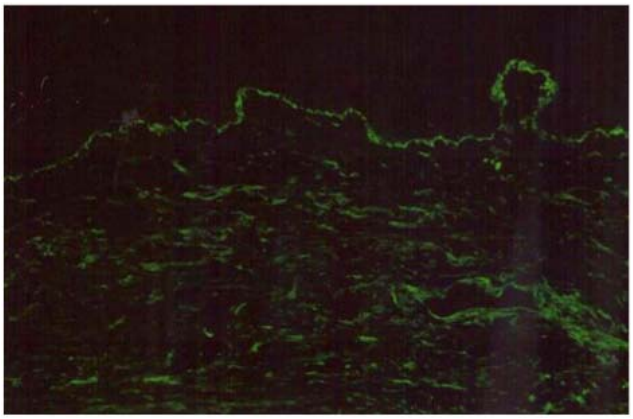

Figure 3: Direct immunofluorescent (IF) study showed linear band of IgG.

MRI (magnetic resonance imaging) with FLAIR (fluid attenuated IR) showed a high dense area of white matter was observed in the peripheral area to the lateral ventricle, suggesting lacuna infarction due to multiple microthrombosis (leukoaraiosis) (Figure **4**). Lacuna infarction in pituitary gland was unclear in MRI. T2WI also showed that punctuated non-signal areas were observed in the cerebral white matter, brainstem site and cerebellum, suggesting multiple microthrombosis (data not shown).

Initially, she was treated with prednisolone (60mg/d intraveneously). The eruptions did not respond to this therapy. Therefore, pulse therapy was commenced with methylprednisolone (500mg/d) for four days with tapering with concomitant use of antimicrobials. The vesico-bullous eruptions subsided gradually, and corticosteroid with predonisolone was tapered to 20mg/d. Afterwards, the patient contracted diabetes mellitus because of the high dose of intake of corticosteroid therapy. Diabetes mellitus was treated with insulin. Finally, the eruptions gradually subsided, resulting in crust and pigmentation. The patient has been treated with predonisolone (20mg/d).

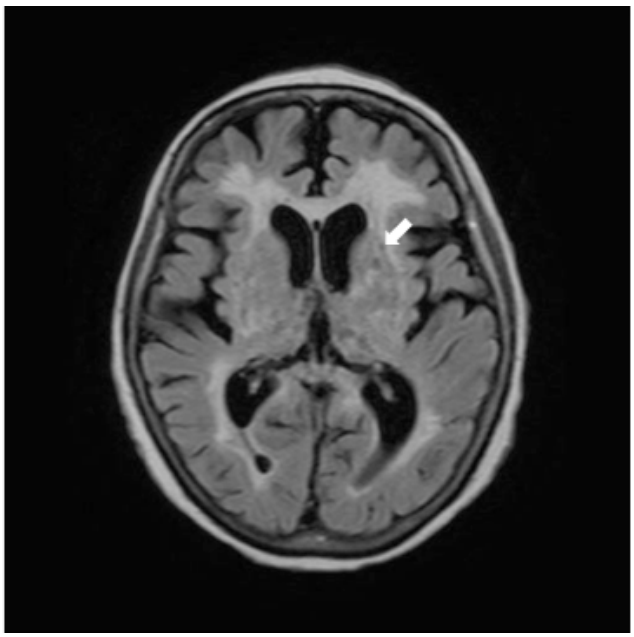

Figure 4: MRI (magnetic resonance imaging) with FLAIR (fluid attenuated IR) showed high dense area in white matter in peripheral area of lateral ventricle, suggesting lacuna infarction due to multiple microthrombosis (leukoaraiosis) (arrow).

At first, edema and slow movement were observed. Thyroid function was examined. The subsequent examinations of endocrine functions were performed. Free T3 (tri-iodothyronin) was decreased (0.91pg/ml), and free T4 (thyroxine) was also decreased (0.44ng/dl). Therefore, hypothyroidism was observed.

To determine the cause of hypothyroidism, pituitary gland function was examined. TSH (0.211 μIU/ml) and adrenocorticostimulation hormone (ACTH) (5.00pg/ml) were decreased. Growh hormone (GH), Luteinizing Hormone (LH) and Follicle stimulating hormone (FSH) were within normal limits. Hypopituitarism was observed and hypothyroidism is diagnosed as secondary type due to hypopituitarism. Adrenal gland function was also examined. Cortisol was within normal limits (12.0μg/dl). Aldosterone was decreased (27.5pg/ml). TSH binding inhibiting immunoglobulin (7.2%) and anti-thyroid peroxidase antibody (7.5 U/ml) were within normal limits. Thyroid hormone and bazedoxifene acetate (vitamin D3) were administered.

DISCUSSION

BP is an autoimmune disease. Antibodies against basement membrane are responsible such as BP180 antibody and BP230 antibody. Autoantibodies can cause BP in mouse models [4]. The high incidence between BP and neurologic disorders (dementia, stroke, Parkinson's disease, multiple sclerosis etc) has been reported [1]. BPAg1 in the intracellular part of hemidesmosome, is cross-reactivity between neuronal antigen and BP antigen (BP230Ab) [1]. In our case, the patient had a history of lacuna infarction 4 years ago earlier prior to onset of BP. Although lacuna infarction in pituitary gland was unclear in MRI, we speculated hypopituitarism is caused by lacuna infarction. BP in a leg affected with hemiparesia has been reported [5].

To investigate the cause of hypothyroidism, pituitary function was examined. Decreased ACTH and TSH showed hypopituitarism. Secondary hypothyroidism due to hypopituitarism was inferred. Next, adrenal gland function was examined. The level of corticosteroid was normal. This may be due to high dose of corticosteroid therapy. Levels of aldosterone were low. The dysfunction of adrenal gland could not be proved because of high dose of corticosteroid therapy. As replacement therapy to supply thyroid hormone, dried thyroid and bazedoxifene acetate were added to her regime.

The etiology of hypopituitarism is considered as tumor, after delivery, inflammation, granulomatous disease, autoimmune disease, iatrogenic disorders and so on [6]. In our case, we speculated lacuna infarction induced hypopituitarism, resulting in secondary hypothyroidism. There has been a report of BP with hypothyroidism having Hashimoto's disease [7]. In our case, TSH binding inhibiting immunoglobulin and anti-thyroid peroxidase antibody were normal. Therefore, Hashimoto's disease was excluded.

We report a case of BP with hypothyroidism caused by hypopituitarism. Multiple endocrine deficiencies (polyglandular failure syndrome) are thought to have an autoimmune disease such as BP [8].

BP should be investigated from endocrine aspects in the future.

CONFLICTS OF INTERESTS

None.

REFERENCES

[1] Langan SM, Groves RW, West J. The relationship between neurological disease and bullous pemphigoid: a population-based case-control study. J Invest Dermatol 2011; 131: 631-6. http://dx.doi.org/10.1038/jid.2010.357

[2] Tsuruta D, Nishikawa T, Yamagami J, Hashimoto T. Unilateral bullous pemphigoid without erythema and eosinophil infiltration in a hemiplegic patient. J Dermatol 2012; 39: 787-9. http://dx.doi.org/10.1111/j.1346-8138.2012.01562.x

[3] Dickmann U, Ritter G, Kretzschmar H. Pemphigoid and cerebral infarct. Syntropy of 2 diseases? Case report. Nervenarzt 1986; 57: 309-10.

[4] Ujiie H, Shibaki A, Nishie W, *et al.* A novel active mouse model for bullous pemphigoid targeting humanized pathogenic antigen. J Immunol 2010; 184(4): 2166-74. http://dx.doi.org/10.4049/jimmunol.0903101

[5] Foureur N, Descamps V, Lebrun-Vignes B, *et al.* Bullous pemphigoid in a leg affected with hemiparesia: a possible relation of neurological diseases with bullous pemphigoid? Eur J Dermatol 2001; 11: 230-3.

[6] Prabhakar VK, Shalet SM. Aetiology, diagnosis, and management of hypopituitarism in adult life. Postgrad Med J 2006; 82: 259-66. http://dx.doi.org/10.1136/pgmj.2005.039768

[7] Callen JP, McCall MW. Bullous pemphigoid and Hashimoto's thyroiditis. J Am Acad Dermatol 1981; 5: 558-60. http://dx.doi.org/10.1016/S0190-9622(81)70116-6

[8] Lynfield YL, Green K, Gopal R. Bullous pemphigoid and multiple autoimmune diseases. Alopecia universalis, bullous pemphigoid, hypothyroidism, rheumatoid arthritis, and neutropenia in one patient. J Am Acad Dermatol 1983; 9: 257-61. http://dx.doi.org/10.1016/S0190-9622(83)80358-2

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